Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

THE DEVELOPMENT OF THE HUMAN EYE

Digitized by Illinois College of Optometry Library

Cambridge University Press
Fetter Lane, London

New York
Bombay, Calcutta, Madras
Toronto
Macmillan

Tokyo
Maruzen-Kabushiki-Kaisha

All rights reserved

Digitized by Illinois College of Optometry Library

THE DEVELOPMENT OF THE HUMAN EYE

BY

IDA C. MANN

M.B., B.S., Lond., F.R.C.S., Eng.

Assistant Surgeon, Royal London Ophthalmic (Moorfields) Hospital; Pathologist, Central London Ophthalmic Hospital; Ophthalmic Surgeon, Elizabeth Garrett Anderson Hospital

With a Foreword by

SIR JOHN HERBERT PARSONS

C.B.E., D.Sc., M.B., F.R.C.S., F.R.S.

CAMBRIDGE

AT THE UNIVERSITY PRESS

Published for

The British Journal of Ophthalmology

1928

Digitized by Illinois College of Optometry Library

LIBRARY
of the
NORTHERN ILLINOIS
COLLEGE OF OPTOMETRY

Carl F. Shepard Memorial Library
Illinois College of Optometry
3241 S. Michigan Ave.
Chicago, Ill. 60616
646

Digitized by Illinois College of Optometry Library

PRINTED IN GREAT BRITAIN

01017

611.84 M31 c.2
24 Jo 49
OD

CONTENTS

Author's Preface *page* vii

Foreword *page* ix

I. The Early Stages of the Formation of the Primary Optic Vesicle

The embryonic plate—The formation of the optic pits *pages* 1–13

II. A General Outline of the Development of the Optic Vesicle and the Associated Mesoderm

The surface ectoderm—The neural ectoderm—The associated mesoderm—The foetal fissure—Abnormalities—Lens formation—Closure of the foetal fissure and further differentiation of the optic cup—The eye at birth *pages* 14–45

III. The Lens

The lens vesicle—The primary lens fibres—The secondary lens fibres—The sutures—The alteration in shape of the lens—Abnormalities *pages* 46–67

IV. The Neural Ectoderm

Pars optica retinae—Stages of differentiation—The closure of the foetal fissure—The development of the *macula lutea* and the *fovea centralis*—*Pars ciliaris retinae*—*Pars iridica retinae*—The *sphincter pupillae*—The *dilatator pupillae*—The optic nerve and chiasmal region—Abnormalities *pages* 68–150

V. The Vitreous and Suspensory Ligament of the Lens

Historical aspect of the problem—First, second and third periods of vitreous development—Cloquet's canal—Postnatal development of the vitreous—Abnormalities *pages* 151–189

Digitized by Illinois College of Optometry Library

VI. The Associated Mesoderm

The foetal blood system and the mesodermal portion of the iris—The development and arrangement of the larger blood vessels in the orbit, supplying or draining the optic cup—The development of the choroid—The development and retrogression of the foetal intraocular blood system—The hyaloid artery—The *tunica vasculosa lentis*—Its three portions and their fate—The differentiation of the vessels of the ciliary body—The development of the definitive retinal arteries and veins—The vessels of the optic nerve—The cilio-retinal artery—Abnormalities—The ciliary muscle—The cornea and sclerotic—The corneo-scleral junction and the angle of the anterior chamber—The lateral and posterior parts of the sclerotic—Abnormalities *pages* 190–252

VII. The Orbit and its Contents

The extrinsic ocular muscles—The head cavities—The capsule of Tenon—The lids and lacrimal apparatus—The position of the eyes *pages* 253–267

VIII. The Phylogenetic Development and Morphology of the Human Eye

The primitive vertebrate eye—Modifications in the Mammalia—In the Sauropsida—Comparison of the retina with other ectodermal derivatives *pages* 268–280

IX. Synoptic Comparison of Ocular with General Development *pages* 281–287

Bibliography *pages* 288–301

Index *pages* 303–306

Figure 109. (Diagrammatic Representation of the Process of Differentiation of the Walls of the Optic Cup)
between pages 132 *and* 133

Digitized by Illinois College of Optometry Library

AUTHOR'S PREFACE

I TAKE the opportunity afforded me by the custom of the Preface to tender my most sincere thanks, in the first place to the Directors of *The British Journal of Ophthalmology* for undertaking the publication of this book, a proceeding obviously involving a serious financial risk, and in the second place to two members of it in particular, to Sir John Parsons for his unfailing encouragement and for the compliment of the Foreword he has written, and to Mr Leslie Paton for his invaluable advice and the trouble he took in reading the proofs. But lastly, to Professor J. Ernest Frazer of the University of London I owe most thanks, not only for the actual material he so generously supplied, without which none of my work would have been possible, but also for the *Lehrjahre* during which he taught me the technical intricacies of embryological research and shewed me a new world beyond the confines of examination syllabuses. If in return I can ever add one fresh observation to the sum of relative knowledge I shall be content.

I offer no justification, other than my own interest in the subject, for having produced a monograph of so limited an appeal as this. Apologies I should perhaps tender for the imperfections of my drawings, though to me they are excused by the pleasure it gave me to make them. By relegating them to a professional artist the book would have gained in appearance but not in originality. I am aware that much work must still be done on the subject. I do not pretend to offer the final word, but merely to present a record of observations which, though incomplete and of necessity largely recapitulatory, have yet the advantage of being direct.

IDA C. MANN

LONDON
February 1928

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

FOREWORD

HITHERTO there has been no comprehensive monograph in English devoted to the Embryology of the Human Eye. General accounts are to be found in most treatises on anatomy and in some treatises on ophthalmology. They are usually somewhat superficial and lacking in detail. Founded chiefly on observations on lower mammals and to an even greater extent on still lower vertebrates, especially birds, they rarely supply adequate information on the events occurring in the developing human eye, and only occasionally record the dates at which important structures first become differentiated. The explanation of most of the congenital abnormalities which are met with depends upon accurate knowledge of normal development, which may tell us whether they are due merely to a so-called abiotrophic arrest or to an arrest due to toxic and other influences, which themselves give rise to complicating structural alterations. The interest aroused by congenital abnormalities has always been striking, and a vast literature has grown up on this subject. In it are scattered many details which have as yet failed to make their way into text-books. Search for such details is a most laborious process, frequently involving the perusal of original papers scattered in anatomical, zoological and ophthalmological journals.

Miss Mann has been peculiarly fortunate in having access to what is probably the most comprehensive series of human embryos available in this country. It has thus been possible to illustrate every stage of human ocular development by an actual specimen, independent of reference to other doubtfully related species. In this way certain debatable points, resting hitherto on comparative observations only, have been placed on a sounder foundation, and certain other processes, for example, those involving growth rates and consequent alteration of position, have been studied for the first time on human material.

Digitized by Illinois College of Optometry Library

The comprehension of rudimentary and vestigial structures calls for some knowledge of comparative embryology, and sufficient reference has been made to phylogenetic development to satisfy this requirement. In the course of the last ten years Miss Mann has devoted a vast amount of time to the study of the comparative embryology of the eye, and I am myself confident that, though much yet remains to be done, she has placed all who are interested in the subject under an obligation in providing them with so exhaustive and well-authenticated a treatise.

JOHN HERBERT PARSONS

February 1928

Digitized by Illinois College of Optometry Library

I

THE EARLY STAGES OF THE FORMATION OF THE PRIMARY OPTIC VESICLE

In order to understand the development of the human eye it is necessary to begin with a clear conception of a very early stage of embryonic life before any of the ocular structures are recognisable. By starting with a comprehension of what might be called a "pre-ocular" stage one can gain a mental picture, not only of the method of production of the human eye, but also of many phenomena connected with the phylogenetic history of the organ.

The embryonic plate. The stage of embryonic development which first concerns us is that in which the future individual is represented by an *embryonic plate* only. This stage, in which the three *primary germinal layers* (ectoderm, mesoderm and entoderm) are present, is common to all vertebrate embryos: it has been more widely studied in the lower animals, in which it is of course easier to obtain specimens in a good state of preservation, than in man.

The stages which lead to the formation of the embryonic plate do not concern us from the point of view of the development of the eye. They have been closely followed in many of the lower mammals, but have never been seen in their entirety in man, though, from the fact that the earliest stage known in man corresponds very closely with a common mammalian stage, it seems justifiable to postulate a similar series of preliminary changes in the human ovum.

It is not intended to describe these early stages in detail, but for the benefit of the student who is unfamiliar with them Fig. 1 has been inserted. It shews in an abbreviated and diagrammatic manner the evolution of the three germinal layers of the embryonic plate from the fertilised ovum of a mammal, and the early differentiation of the plate. The embryonic plate stage, to the formation of which all these changes tend, is well known in man, and will now be described.

Fig. 2 *A* gives a diagrammatic representation of the interior of an ovum (such as that in Fig. 1 *E*). The upper surface of the embryonic plate, the amnion having been removed, is seen in Fig. 2 *B*. Fig. 2 *C* shews a transverse section through the centre of the embryonic plate at right angles to its long axis (in the situation indicated by the arrow in Fig. 2 *B*).

Digitized by Illinois College of Optometry Library

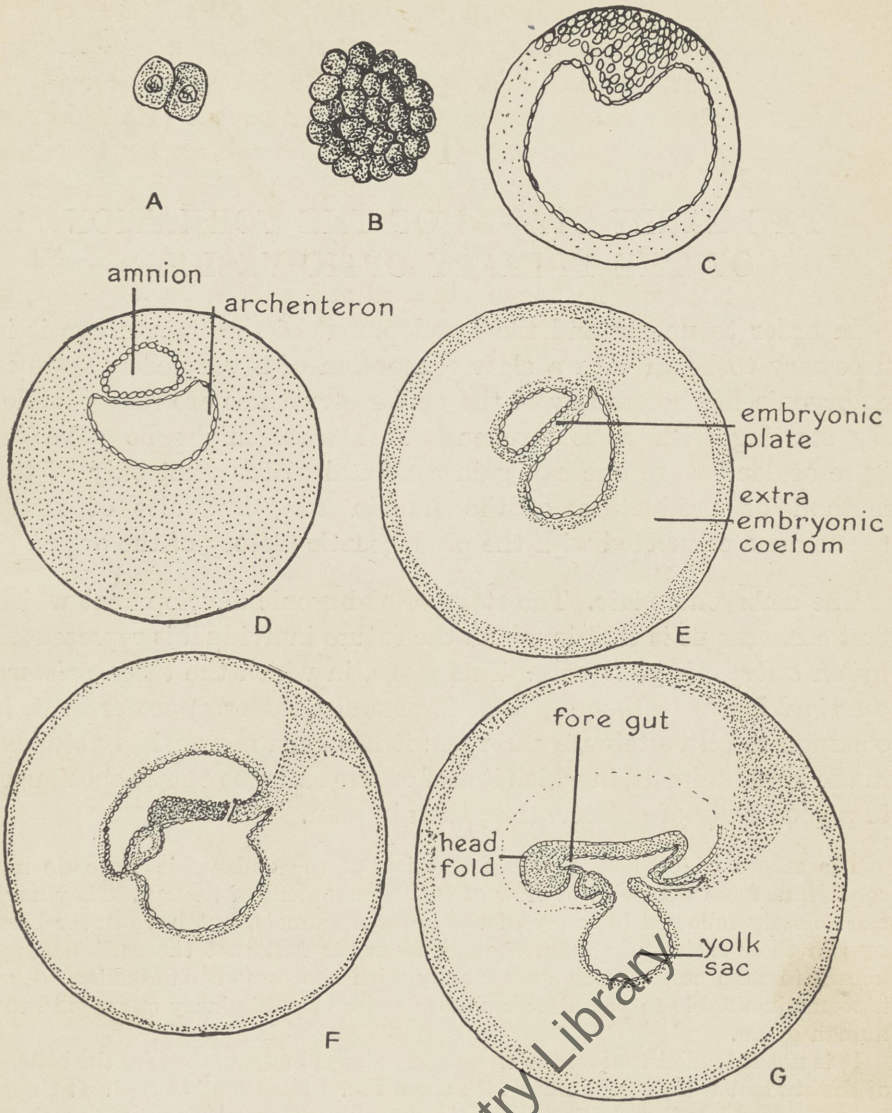


Fig. 1. Diagrams shewing the evolution of the three germinal layers of the embryonic plate from the fertilised ovum of a mammal and the early differentiation of the plate. *A*, first division in the segmentation of the fertilised ovum. *B*, final division producing the *morula stage*, a solid mass of cells known as *blastomeres* or *segmentation cells*. *C*, conversion of the morula into a hollow sphere, known as the *blastula* or *blastocyst*, the cells of the upper pole of which divide to form the *inner cell mass*. *D*, appearance of the *amniotic* and *archenteric* cavities. The ovum is now filled with cells, constituting the extra-embryonic mesoblast, in which are two cavities, the upper one, lined by epiblast, being the amniotic cavity, and the lower one, lined by hypoblast, the archenteric cavity. *E*, a split now occurs in the extra-embryonic mesoblast, a cavity, the *extra-embryonic coelom*, being thus produced. Mesoblast (the *intra-embryonic mesoblast*) has now appeared between the epiblast and hypoblast where they were previously in contact, so that an *embryonic plate* consisting of the three germinal layers can now be recognised. The embryonic plate with its amnion and archenteron is attached to the wall of the ovum by means of the *body stalk*. *F* and *G* shew differentiation of the embryonic plate, the appearance of head and tail folds, the formation of the fore and hind guts and the body stalk. For further description of the embryonic plate see text.

Digitized by Illinois College of Optometry Library

The three germ layers (ectoderm and entoderm with mesoderm between them[1]) are seen superimposed. Running longitudinally in the centre of the embryonic plate is a short groove, the *neural groove*, bounded on either side by low prominences, the *neural* or *medullary ridges*; the ectoderm covering these ridges is thickened. (An ovum

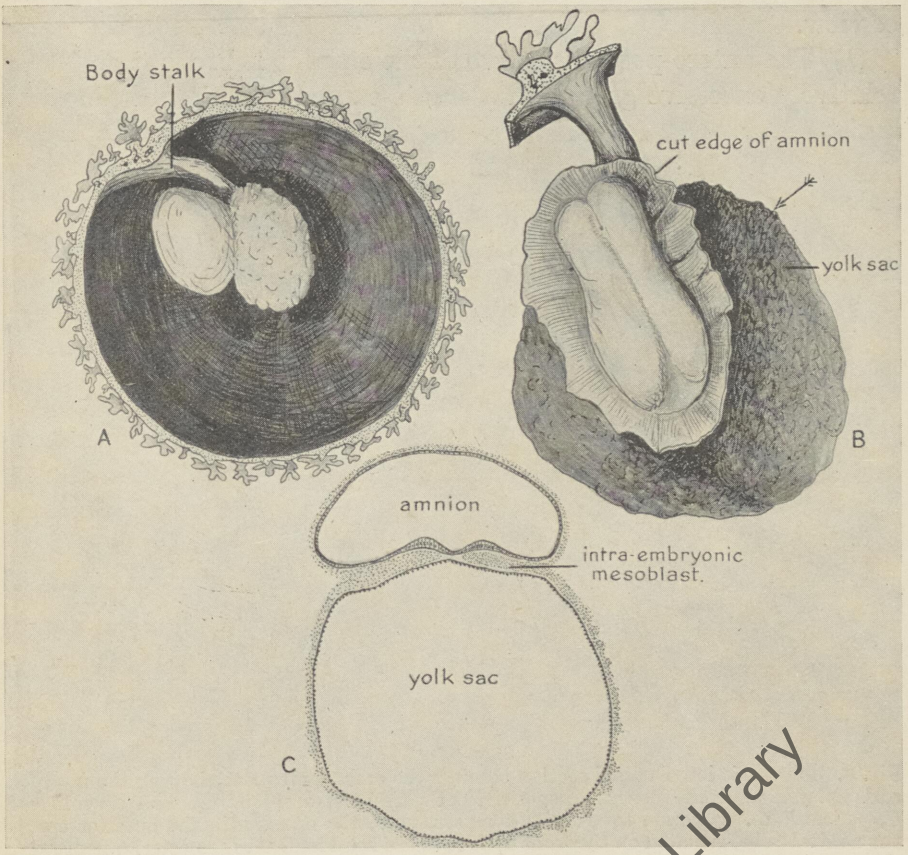


Fig. 2. Diagrams representing the embryonic plate stage of development. *A* shews the interior of the ovum, the *embryonic plate*, *amnion* and *yolk-sac* hanging attached to the wall of the ovum by the *body stalk*. *B*, the upper surface of the embryonic plate of a slightly older specimen than that in *A*. The amnion has been removed. *C*, a transverse section of the plate at the point marked by the arrow in *B*.

of this stage is in the 3rd week of development and the embryonic plate measures between 1 and 2 mm. in length.)

In the caudal half of the embryonic plate is a small passage (the *neurenteric canal*) communicating with the cavity of the yolk sac. This does not concern us.

[1] The terms mesoblast, epiblast and hypoblast are used for the three germ layers up to the beginning of differentiation. After this the terms mesoderm, ectoderm and entoderm are substituted.

Digitized by Illinois College of Optometry Library

Towards the cephalic (anterior) end of the plate the *neural groove* widens out and its two margins diverge somewhat (Fig. 2 *B*).

The relatively flat embryonic plate becomes converted into the rounded and curved form of the embryo as a result of relatively different rates of growth of the various portions of the cell layers composing the plate: it is necessary to consider this from two points of view.

(1) The antero-posterior curve of the embryo is brought about by relatively excessive growth in a cranio-caudal direction of the walls

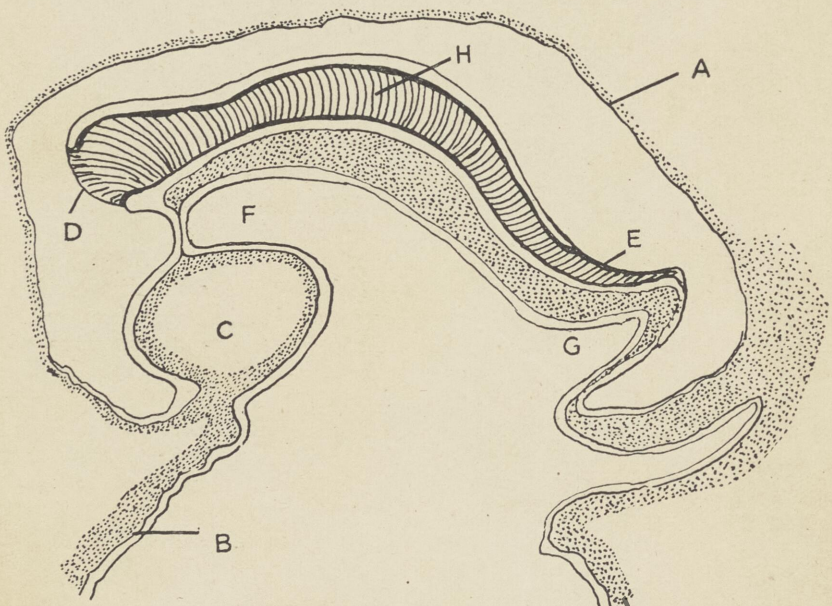


Fig. 3. Schematic longitudinal section through the embryonic plate shewing the *head fold* and *tail fold* and the general disposition of parts. *A*, amnion. *B*, wall of yolk sac. *C*, pericardium. *D* points to the anterior neuropore, the opening in the anterior end of the neutral tube, situated on the front surface of the head fold. *E*, the posterior neuropore, the opening at the posterior end of the neural tube. *F*, the fore-gut. *G*, the hind-gut. *H*, the neural tube.

of the neural groove: the growth of the mesoderm in the plate keeps pace with this more or less.

This excessive growth rate causes the anterior and posterior ends of the neural region to project beyond the corresponding margins of the plate, folding under themselves in doing so the structures originally lying between them and these margins (Fig. 3). In this way the projections called the *head* and *tail folds* are produced.

The plate stands up into the amniotic cavity and projects over its own original margins: the projection is best marked at the cranial end and least marked at the sides. The cranial and caudal projections

Digitized by Illinois College of Optometry Library

enclose diverticula of the yolk sac, known as the *fore-* and *hind*-guts respectively. The *fore-gut* is therefore an entodermal recess lying below the front portion of the neural groove.

(2) The neural groove not only grows in length *pari passû* with the longitudinally extending mesoderm, but even exceeds this so that its anterior end projects forwards markedly beyond the general level of the other structures, and is somewhat turned down here. The projection is really caused, of course, by growth of the neural ridges (Fig. 4) which stand out in this situation with the neural groove between them widely open forwards. At their anterior and lower ends these two ridges, converging slightly, fade away. It is this anterior region of the rudiment of the central nervous system which gives origin to the *paired optic outgrowths*.

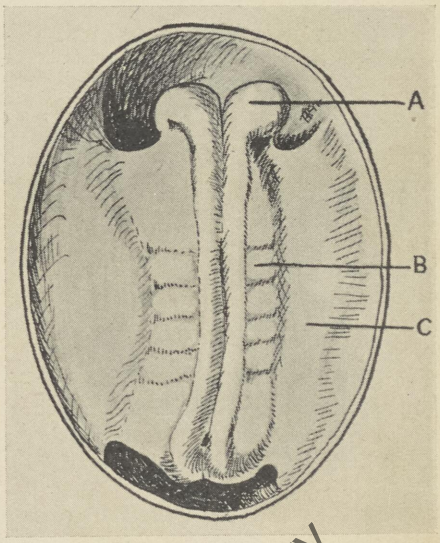


Fig. 4. Surface view of the embryonic plate before closure of the neural tube. (After Keibel.) *A*, anterior end of neural ridge. *B*, paraxial segmented mesoderm. *C*, lateral sheet of mesoderm.

Before proceeding to deal further with this part of the nervous system it is necessary to describe shortly the disposition of *mesoderm* in the embryonic plate. The general mesodermal layer throughout the plate can be divided—as is indicated on the surface by a longitudinal groove—(Fig. 4) into:

(*a*) A *medial* part, underlying to a great extent the neural ridges and so lying beside the neural groove and hence called the *paraxial mesoderm* (this is shewing segmentation) and

(*b*) A *lateral* sheet, extending outwards from this to the margin of the plate. When the fore-gut is formed by the growth of the head fold, its side wall contains *lateral* mesoderm, while the *paraxial* (medial) portion of the mesoderm lies beside the neural structures in its roof.

As the enlargement of the projecting portion of the neural ridges makes a definite brain formation at the cranial end, the mesoderm covering it in a thin layer is derived, as is easily understood, from the *paraxial* portion. The *visceral arches* (so-called "branchial" arches) of the pharyngeal wall are as evidently formed from mesoderm belonging to the *lateral* sheet: consequently the structures developed in this layer are frequently termed "visceral" and the same name

Digitized by Illinois College of Optometry Library

may be employed in speaking of the mesodermal layer itself, so that in the head region the two mesoderms can be identified as *paraxial* and *visceral* respectively.

The *paraxial* mesoderm is remarkable in that it shews a definite metameric segmentation, which begins in the central region.

These segmental masses are increased rapidly in number by addition from behind and their appearance (Fig. 4) is quickly followed by closure of the neural groove, the groove being thus converted into a tube. The paraxial mesoderm which extends forwards beside the growing brain does not however shew this segmentation, although it can be recognised as distinct from the lateral unsegmented sheet. This absence of segmentation of the paraxial mesoderm in the head region is a character which has probably been acquired during phylogeny.

Each little segment of the paraxial mesoderm is known as a *somite* or *myotome*. It consists of cells arranged to form the wall of a small cavity, the *myotome cavity*, which is completely closed. From the walls of the myotome cavity are formed the skeletal supports for the derivatives of the neural plate and also the musculature of the body wall.

In the head region the metameric arrangement has been lost, in association with the condensation in phylogeny of several segments in this part. In some of the lower vertebrates, a few of the condensed myotomes taking part in the formation of the skull can be recognised in early stages and small cavities (the *head cavities*), corresponding and in series with the myotome cavities along the rest of the body, can be demonstrated as transient phenomena. From the walls of these head cavities are formed in the same way skeletal and supporting structures, including the orbital muscles (see Section VII *a*). In man attempts have been made to prove the presence of head cavities but very little is known of them definitely.

The Formation of the Optic Pits

The neural groove deepens and, as already said, begins to close over in its central part, as illustrated in Fig. 5.

The anterior end is still widely open, the neural ridges on either side forming prominent convex masses. Owing to this projection the end of each ridge, originally anterior, is now turned on to the under surface of the head. The two ends of the neural ridges approximate, fuse and so form a low transverse fold (the *anterior neural fold*) at the termination of the open groove (see Fig. 6). As the ridges grow this fold also increases in height so that a little recess is formed behind it marking the end of the open groove, and on each side this small recess terminates in a commencing depression of the surface of the neural ridge: these two lateral depressions are the optic pits.

To follow the relations of the optic pits, it must be understood that the cranial projections of the neural ridges are largely produced by the thickening and rapid proliferation of the ectoderm on their

Digitized by Illinois College of Optometry Library

neural surfaces. Mesoderm underlies each ridge and extends for a considerable distance into it, but the free edge or crest of each ridge has no room for mesoderm owing to the thickening of the neural ectoderm. It has already been pointed out that the crests of the neural ridges turn downwards in front, and the ridges become lower, and at the level of the fossa just behind the anterior neural fold there is practically no mesoderm at this stage. The neural ectoderm on the inner side of the fold is in direct contact with the unthickened surface ectoderm externally.

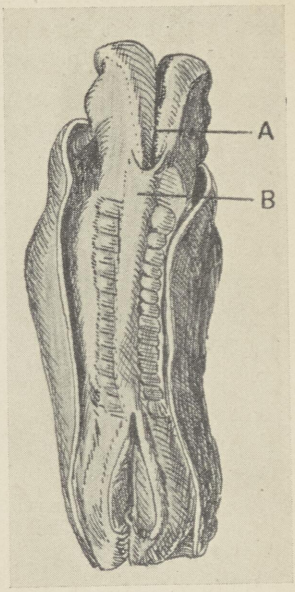


Fig. 5. Embryo 2·11 mm. in length (after Eternod) shewing closure of the neural groove in its central part. *A*, open portion of neural groove. *B*, closed portion of neural groove.

The optic pits are symmetrical and paired from the first. It has been suggested that the eye was originally median, but there seems to be no conclusive support for this view. In Ascidians a single median eye is found, but it has been shewn (Froriep) that this is probably the surviving right-hand member of an original pair, and one must not consider the Ascidian larva as on the direct phylogenetic line of the vertebrates.

The optic pits are thus lateral out-pouchings of the front end of the neural plate. They involve that portion of the neural ectoderm of the upper surface of the head fold which is in direct contact with the surface ectoderm.

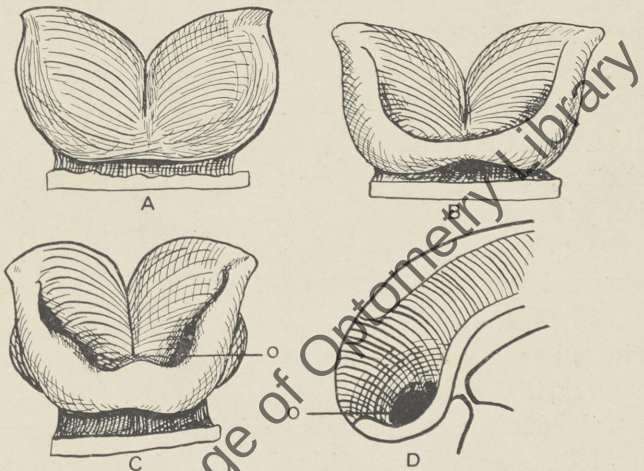


Fig. 6. Scheme shewing the development of the *optic pits* at the anterior part of the *neural ridges*. *A*, anterior end of fore-brain before appearance of optic pits. *B*, first appearance of transverse ridge uniting neural ridges. *C*, optic pits shewing on either side behind transverse ridge; *o* = optic pit. *D*, median longitudinal section of a stage a little later than *C*, shewing partial dorsal closure of the tube; *o* = optic pit.

Digitized by Illinois College of Optometry Library

Fig. 7 shews a horizontal section through the optic pits in a human embryo of 2·6 mm. Fig. 8 shews a surface view of a model of the head end of a pig embryo (after Keibel and Mall). Fig. 9 *A* shews a model, and Fig. 9 *B* a section of a guinea-pig embryo of the same stage.

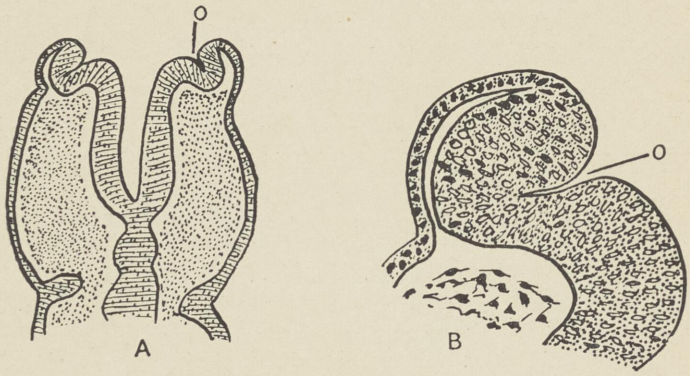


Fig. 7. Sections through the optic pits (*o*) of a 2·6 mm. human embryo (after Keibel and Mall). *A*, low power, and *B*, high power.

This stage is suggestive if one appreciates the fact that the neural tube is still open and so the optic pits are also open externally, i.e. they are ectodermal depressions on the surface of the body. Thus they now resemble in some particulars the sensory *placodes* which are found on the head of the embryo in connection with some of the cranial nerves (e.g. the 7th, 8th, 9th and 10th). A placode is essentially a thickened, often depressed portion of the surface ectoderm which subsequently sinks in and becomes cut off from the surface, giving rise to, and gaining connection with, some of the cells of the ganglion of an afferent cranial nerve. The optic pit differs from other placodes in an important particular, namely, that although it arises on the surface of the embryo, it involves that portion of the ectoderm which is neural and will subsequently become shut off from the surface of the body by the closure of the neural tube. Thus the optic placode is carried mechanically into the interior of the central nervous system and does not sink in from the surface to join this

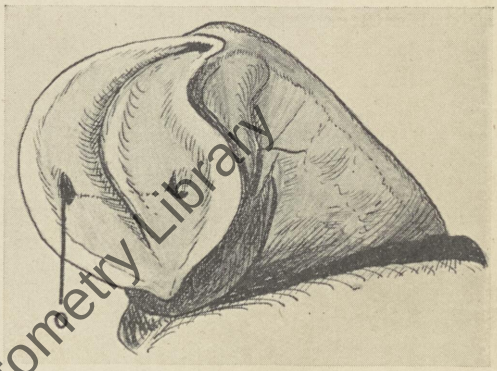


Fig. 8. Model of anterior end of pig embryo shewing commencing optic pits (after Keibel and Mall); *o* = optic pit.

Digitized by Illinois College of Optometry Library

secondarily. For this reason the optic pit cannot be considered a true placode[1].

We may here anticipate matters somewhat by pointing out that those cells which form the floor of the optic pit will finally differentiate into the percipient elements of the finished sense-organ, i.e. the rods and cones of the retina. It is extremely interesting to note that whereas in the definitive eye the layers of bipolar and ganglion cells and of nerve fibres lie between the rods and cones (the percipient elements) and the light which stimulates them, at this stage they are exposed directly to the light, i.e. on the surface of the body, the other (conducting) layers of the sense-organ lying *in posse* deep to them and further from the light. This arrangement appears more

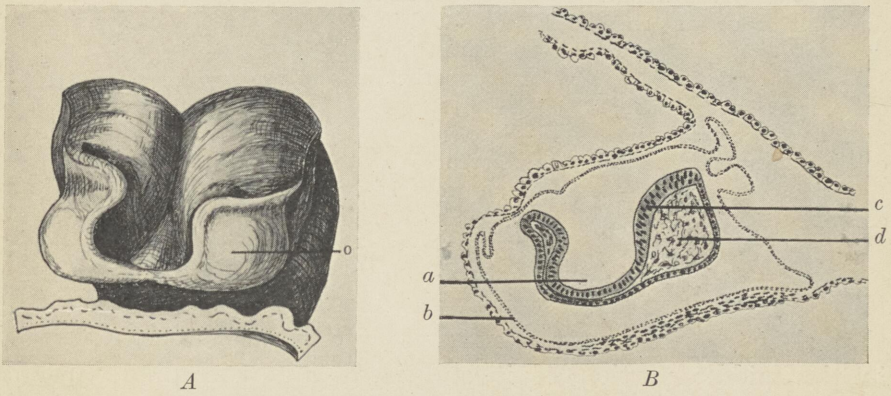


Fig. 9. Optic pits of guinea-pig embryo. *A*, model of anterior end of embryo: the left optic pit is deep to the protrusion at *o*. *B*, section through one optic pit shewing area of direct contact between surface and neural ectoderm. *a*, floor of optic pit; *b*, amnion; *c*, neural ectoderm; *d*, mesoderm.

simple and straightforward than the final reversed structure, and is found in the adult stage of certain invertebrates which possess simple eyes (e.g. Sepia).

It might therefore be said that possibly the vertebrate eye, which is essentially a cerebral eye, might have arisen by the inclusion of that part of the surface of the body, which originally bore the optic placode or simple eye, within the area of (neural) ectoderm which sinks in and becomes buried as the central nervous system. This burial of the eye removes it from the light, and it must therefore

[1] Attempts have been made (Dendy, Dareste) to shew that the optic pit develops first in what is apparently surface ectoderm and is only secondarily converted into neural ectoderm by growth and closure of the nerve tube. If this were so, the analogy to the other sensory placodes would be more perfect, but later observers are of the opinion that the area involved in the formation of the optic pits in mammals is definitely neural from the first.

Digitized by Illinois College of Optometry Library

grow outwards from the wall of the central nervous system until it abuts against the surface ectoderm and so reaches the light again. It is, however, convex towards this surface and is therefore not well adapted to its function and so undergoes a secondary invagination in order to become concave towards the light. This change of shape and position produces an efficiently formed organ but has the (slight) disadvantage that it leads to the reversal of the retinal layers, the percipient elements still remaining turned towards the cavity of the central nervous system (the original surface of the body) and not towards the cavity of the eye itself.

This method of development, namely the production of a cerebral eye, is found without exception in all vertebrates. In Amphioxus the eye is very rudimentary, being represented by a "pigment spot" only, while in the Ascidian larva the secondary outgrowth of the optic vesicle towards the surface does not occur and the eye is embedded in the central nervous system and turned towards the cavity of the brain tube.

With regard to the question of whether an optic placode can be said to exist, one must also mention that attempts have been made to homologise not the optic pit but the lens thickening of the surface ectoderm with the other epibranchial placodes[1] of the embryo.

Our knowledge of phylogeny is, however, far too incomplete to allow of any certain statement on the matter.

After the 2·6 mm. stage (Fig. 7) described above, growth is fairly rapid along the edges of the neural plate. We have seen that closure of the central nervous system has already occurred in the middle portion of it and is rapidly spreading upwards and downwards. The wide-open anterior end is the last to close. By the 3 mm. stage, only a small portion at the anterior end (the anterior neuropore) remains open: this closes almost immediately afterwards.

Fig. 10 shews a reconstruction of a 3·2 mm. human brain.

The *optic pit* is now seen as a deepening depression in the lateral wall of the fore-brain slightly towards its ventral aspect. Seen from the outer aspect of the brain tube, the depression of the optic pit appears as a rounded projection which springs from the ventro-lateral aspect of the brain and projects slightly backwards. It is now known as the **optic vesicle**. It increases in size, and becomes more spherical, and by 4 mm. has the appearance seen in Fig. 11.

This 4 mm. embryo possesses a definite head, body and tail; its central nervous system is completely closed off from the amniotic cavity, and the main divisions of it can be recognised, namely a

[1] Brachet.

Digitized by Illinois College of Optometry Library

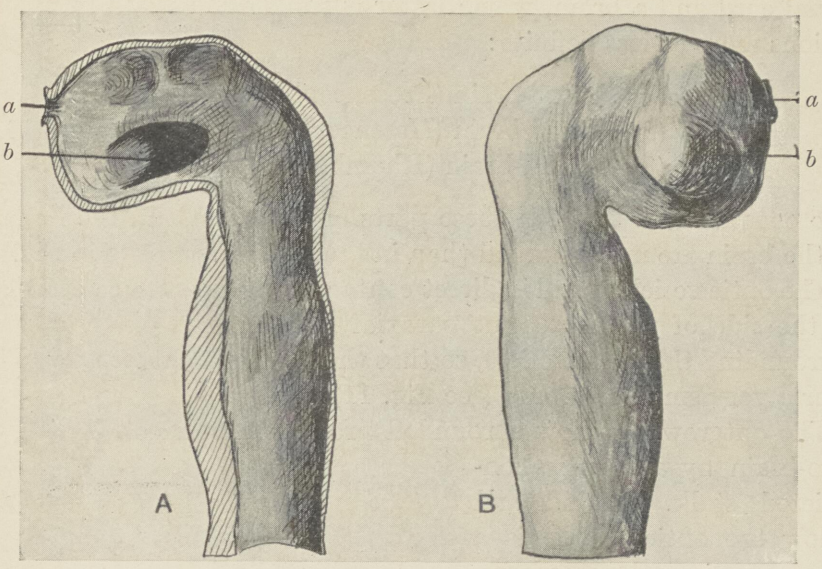


Fig. 10. Reconstruction of the brain of a 3·2 mm. human embryo (after His). *A* shews the interior and *B* the exterior of the neural tube. *a*, anterior neuropore; *b*, optic outgrowth. The upper flexed portion is the *fore-brain* and the optic outgrowth projects from this. The fore-brain is connected by a short curved *mid-brain* with an elongated *hind-brain*.

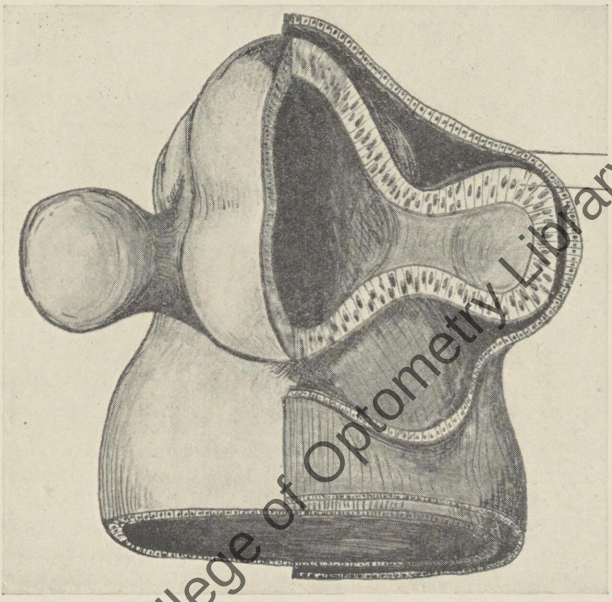


Fig. 11. Model of fore-brain and optic vesicles of a 4 mm. human embryo seen from the front. The optic vesicle on the left of the embryo is represented in section. *a*, surface ectoderm; *b*, neural ectoderm.

Digitized by Illinois College of Optometry Library

spinal cord and a brain, which latter is subdivided again into three regions more or less definite:

(1) A fore-brain (Prosencephalon).
(2) A mid-brain (Mesencephalon).
(3) A hind-brain (Rhombencephalon).

The constrictions between these parts of the brain and the flexures of the brain are more marked than in the 3·2 mm. embryo in Fig. 10.

The optic vesicle is still in direct contact with the surface ectoderm at the side of the head, but paraxial mesoderm is extending and surrounding the optic vesicle, so that the original contact now exists over a very small area only (see Fig. 11).

The outgrowth is now a rounded protrusion connected with the fore-brain by a slightly constricted stalk. Behind and below the optic vesicle is a mass of visceral mesoderm, the *maxillary process*. This, further back, is continued into the 1st pharyngeal arch (*mandibular*). The *maxillary process* (on each side) grows forward by subepithelial extension[1] on the under surface of the head, deep to the anterior end of the fore-brain and the optic vesicle growing from it. Thus the developing eye, although surrounded by paraxial mesoderm, is being supported, as it were, on a lateral shelf or bracket of visceral mesoderm (see Fig. 12). From this stage onwards one can recognise the definite rudiment of the eye, and the further story of its development is the story of the differentiation of the optic vesicle together with that of the covering surface ectoderm, the surrounding paraxial mesoderm and the supporting maxillary mesoderm.

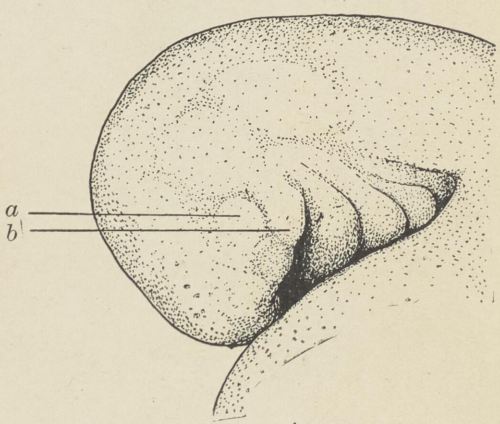


Fig. 12. Diagram shewing the side view of the head of a 4·5 mm. human embryo. The optic vesicle is situated at *a* and the maxillary process at *b*.

In describing stages of development in the human embryo, in which exact data as to time of fertilisation of the ovum are impossible to procure, it will

[1] It must be understood that the mesoderm of the maxillary process is *not* separated from the paraxial mesoderm above it by epithelium (Fig. 15). The two mesodermal condensations are in contact though they do not fuse. It is a common error to suppose that the maxillary process, covered by ectoderm, is applied to the ectoderm of the surface of the head, and on this assumption has been founded an "explanation" of the occurrence here of so-called dermoids. There is no foundation for this assumption.

Digitized by Illinois College of Optometry Library

be found more convenient and more accurate to name the stage according to the length of the embryo rather than to its reputed age. For one thing, the reputed age, even though correct, does not necessarily give us the exact stage of development, since embryos, like adults, are subject to slight variations in their rate of development, and two embryos known to be of the same age are not necessarily of the same size. On the other hand, the stage of development reached for a certain length is much more constant, and one therefore names the stages in millimetres of length rather than days of development. The length measured is the distance from end to end of the embryo. It is not uncurled and the measurement is taken from point to point direct, not along the convexity of the curve. In older foetuses the length is the rump-vertex measurement or "sitting height," no account being taken of the legs. All specimens should be measured fresh, not after embedding, as they shrink considerably during the process.

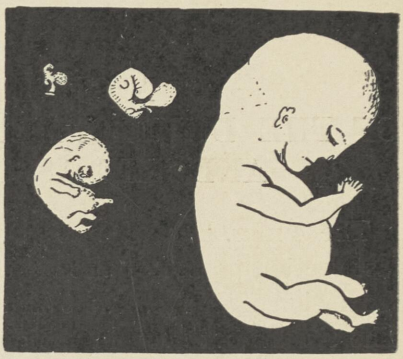


Fig. 13. Diagrams shewing the surface form of embryos at various stages drawn natural size. Embryos of 2·5, 6·5, 13 and 36 mm. respectively.

It is, however, useful to have some arbitrary method of arriving at the connection between the length and the probable age of the specimen, and for this purpose the following rule will be found the simplest and most accurate.

1. After the 1st month and up to the 3rd. The embryo will be less than 70 mm. in length. The age in days is given by the formula:

$$\sqrt{\text{length in mm.} \times 100} = \text{age in days.}$$

2. To determine the age of a foetus of more than 70 mm. in length.

Taking the age at 70 mm. as 3 months, one can consider that 10 mm. per week are added from 3 months up to term. The formula would then be:

$$12 + \frac{\text{length in mm.} - 70}{10} = \text{age in weeks.}$$

A list of age-length relationships[1] at representative stages is added for reference:

4 weeks (28 days)	7·8 mm.	11 weeks (77 days)	59·2 mm.
5 ,, (35 ,,)	12·2 ,,	12 ,, (84 ,,)	70·5 ,,
6 ,, (42 ,,)	17·6 ,,	18 ,,	130 ,,
7 ,, (49 ,,)	24 ,,	24 ,,	190 ,,
8 ,, (56 ,,)	31·3 ,,	30 ,,	250 ,,
9 ,, (63 ,,)	39·6 ,,	36 ,,	310 ,,
10 ,, (70 ,,)	49 ,,	39 ,,	340 ,,

In order to give a slight idea of the alteration in general external form of the embryo during growth, a diagram is added shewing embryos of various ages (Fig. 13) drawn actual size.

[1] It is recognised that the various measurements given are not in accord with many modern computations, especially with regard to the earlier stages.

Digitized by Illinois College of Optometry Library

II

A GENERAL OUTLINE OF THE DEVELOPMENT OF THE OPTIC VESICLE AND THE ASSOCIATED MESODERM

The 4 mm. human embryo (Fig. 14) described at the end of the last section possesses already the principal structures involved in the formation of an eye. These structures are as yet entirely unspecialised. The tissues involved in the development of the eye can be broadly classified under the headings:

Surface ectoderm.
Neural ectoderm.
Associated mesoderm.

The surface ectoderm concerned in the formation of the eye is that portion of the ectodermal covering of the embryo which is in rela-

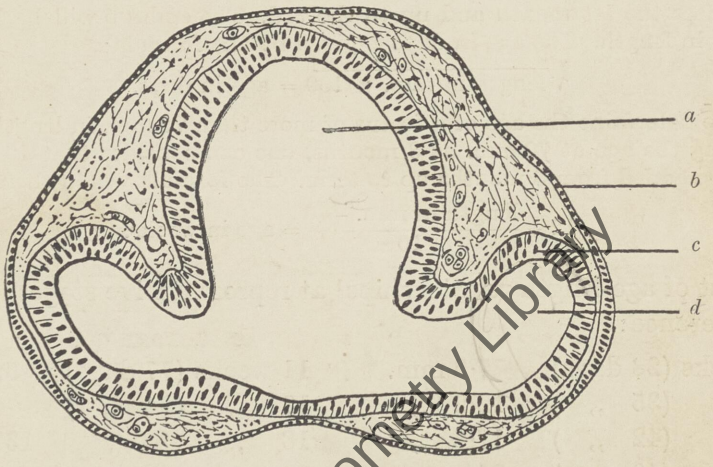


Fig. 14. Transverse section through anterior part of fore-brain and optic vesicles of a 4 mm. human embryo (after Seefelder). *a*, cavity of fore-brain; *b*, surface ectoderm; *c*, wall of optic vesicle; *d*, cavity of optic vesicle.

tion with the primary optic vesicle. At this stage it differs in no way from that covering the rest of the head and body of the embryo, save that, as has already been pointed out, it is in one place in direct apposition to the neural ectoderm of the primary optic vesicle, no mesoderm intervening, whereas elsewhere surface ectoderm is always separated from the brain by mesoderm. From this portion of surface

Digitized by Illinois College of Optometry Library

ectoderm (the area in contact with the optic vesicle with a small surrounding area) will develop the lens, and the epithelial covering of the cornea, conjunctiva and lids, and the epithelial structures associated with the lids, namely hairs and glands.

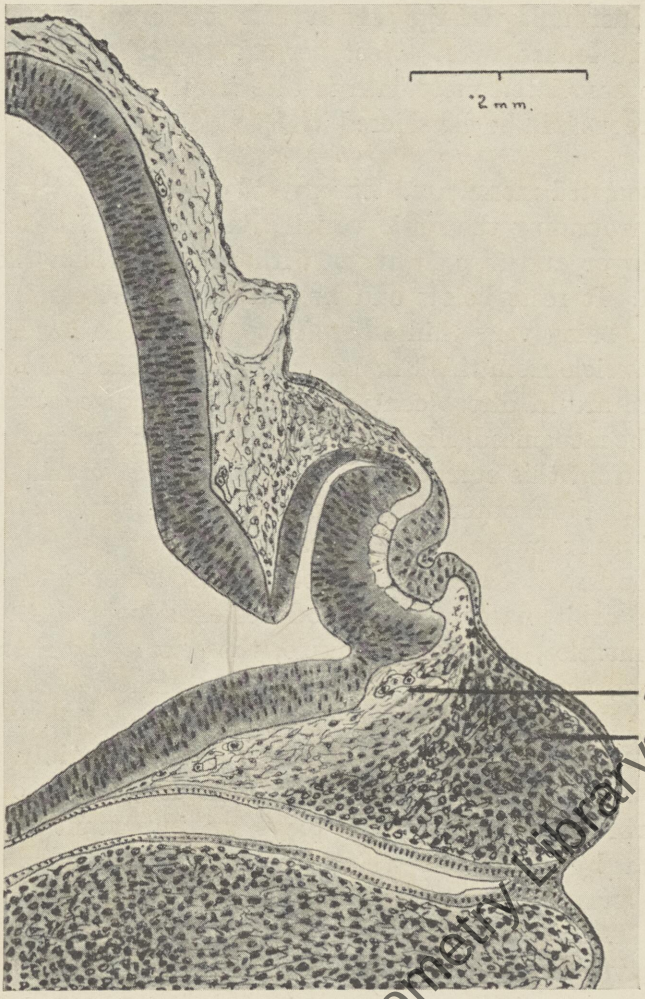


Fig. 15. Transverse section through the optic vesicle and maxillary process of a 5 mm. human embryo. *a*, visceral mesoderm of maxillary process; *b*, paraxial mesoderm.

The neural ectoderm is that which composes the wall of the primary optic vesicle. It is directly continuous with the ectoderm of the fore-brain and hence with the walls of the whole central nervous system, and like them is entirely unspecialised at this stage. From this neural ectoderm will be formed the retina, the pigment epithelium of the retina and of the ciliary processes and posterior layers

Digitized by Illinois College of Optometry Library

of the iris, the sphincter and dilatator pupillae muscles and the optic nerve.

With regard to the formation of the vitreous humour and of the suspensory ligament of the lens, all that can be said at this stage is that protoplasmic adhesions between the surface ectoderm and the neural ectoderm play a large part in their development, and therefore they can be looked upon as ectodermal in origin. The amount to which the associated mesoderm is also involved in the production of the vitreous will be considered in detail later.

The associated mesoderm. The mesoderm immediately and completely surrounding the optic vesicle, and its stalk, belongs to the paraxial layer and is continuous with that in which the brain is embedded. It rests below and behind on the (visceral) maxillary mesoderm, being very thin where it separates the lower aspect of the optic vesicle from this "maxillary" tissue. The two mesodermal strata here are in direct contact, but the line of contact between them can be recognised (Fig. 15). The orbit with its related structures is formed from this surrounding mesoderm. The maxillary process makes its floor and outer wall, the rest of its boundaries and contents being derived from the paraxial stratum.

From the associated **paraxial mesoderm** are developed the structures within the orbit, namely, the blood vessels supplying the eye, the extrinsic muscles, the ciliary muscle, the sclera, the sheath of the optic nerve, the various connective tissue structures in the orbit and nearly the whole of the inner and upper bony wall.

The **visceral mesoderm** (maxillary process) is mainly concerned with the formation of the bones of the lower and outer walls of the orbit. Its growth also plays an important part in the mechanism by means of which decrease in the angle between the optic axes is brought about. This mechanism is explained in Section VII.

The derivation of the various parts of the fully formed eye from the three types of tissue recognisable at 4 mm. can therefore be tabulated as follows:

Surface ectoderm gives rise to:

Lens.
Epithelium of cornea.
Epithelium of conjunctiva (and hence) lacrimal gland.
Epithelium of lids and its derivatives, the cilia, the Meibomian glands and the glands of Moll and Zeiss.
Epithelial lining of lacrimal apparatus.

Digitized by Illinois College of Optometry Library

Neural ectoderm gives rise to:

Retina with its pigment epithelium.
Epithelium covering ciliary processes.
Pigment epithelium covering posterior surface of iris.
Sphincter and dilatator pupillae muscles.
The optic nerve (neuroglial and nervous elements only).

Adhesions between surface and neural ectoderm give rise to:

Vitreous.
Suspensory ligament of lens.

Associated paraxial mesoderm gives rise to:

The blood vessels, i.e. the choroid, the arteria centralis retinae, ciliary vessels, and other vessels of the orbit which persist, as well as the hyaloid artery, the vasa hyaloidea propria, and the vessels of the vascular capsule of the lens which disappear before birth.
The sclerotic.
The sheath of the optic nerve.
The ciliary muscle.
The substantia propria of the cornea and the endothelium of its posterior surface.
The stroma of the iris.
The extrinsic muscles of the eye.
The fat, ligaments and other connective tissue structures in the orbit.
The upper and inner walls of the orbit.
The connective tissue of the upper lid.

Visceral mesoderm (maxillary process) below the eye gives rise to:

The lower and outer walls of the orbit. The structures lying behind and below the eye (i.e. the ali-sphenoid, malar and orbital plate of superior maxilla).
The connective tissues of the lower lid.

The separate structures are dealt with in detail in Sections III to VII; it is convenient at this stage to consider the general scheme of growth, and the more important changes of gross form which occur during development.

The Surface and the Neural Ectoderm

The drawing seen in Fig. 16 represents the surface form of the fore-brain and optic vesicles of a 4 mm. embryo seen from in front and below. On the right side of the embryo the optic vesicle is represented complete and the surface ectoderm has been removed. On the left side the surface ectoderm is shewn but it and the fore-brain and optic vesicle have been cut in coronal section so that their thickness can be seen, and also the interior of the cavity of the fore-brain. This is continuous by a wide opening (the cavity of the optic stalk) with the cavity of the optic vesicle, which is roughly spherical and projects laterally from the lower and posterior part of the fore-

Digitized by Illinois College of Optometry Library

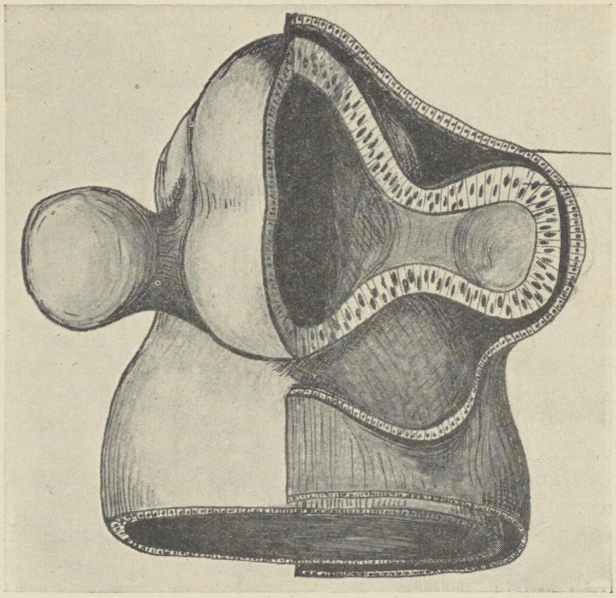


Fig. 16. Model of fore-brain and optic vesicles of a 4 mm. human embryo seen from the front. The optic vesicle on the left of the embryo is represented in section. *a*, surface ectoderm; *b*, neural ectoderm. Note thickening of former to form lens plate.

brain vesicle. A single coronal cut will at this stage open both optic vesicles and their communication with the fore-brain cavity, so that

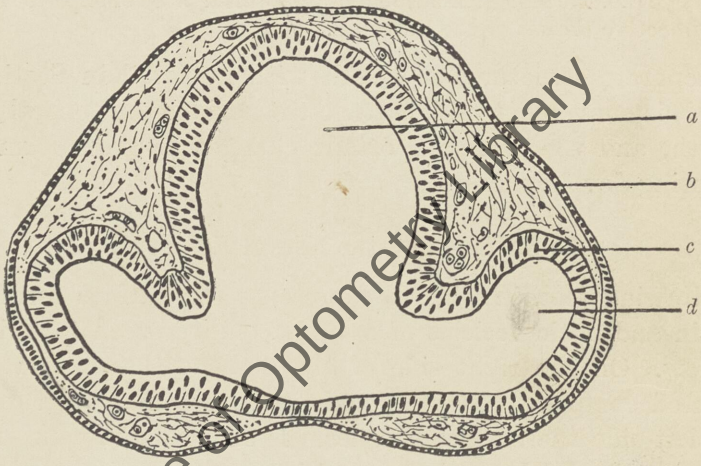


Fig. 17. Transverse section through anterior part of fore-brain and optic vesicles of a 4 mm. human embryo (after Seefelder). *a*, cavity of fore-brain; *b*, surface ectoderm; *c*, wall of optic vesicle; *d*, cavity of optic vesicle.

the axes of the two eyes lie in the same straight line and there is no angle between the optic stalks (Fig. 17).

Digitized by Illinois College of Optometry Library

The surface ectoderm forms a thin covering which on the top of the head is almost in contact with the fore-brain. It is applied laterally to the optic vesicle and over the most prominent part of the latter is in direct contact with it. Below the eye it curves away from the neural ectoderm to cover the small maxillary process, and then passes upwards again to lie in direct contact with the under surface of the fore-brain in the middle line. This is the situation of Rathke's pouch and the future pituitary body.

Fig. 18 shews the side view of the same region after removal of the ectoderm and the mesoderm. The flexure of the fore-brain can be better appreciated from the side, and also the relation of the optic outgrowth to the lower and back part of the sides of the fore-brain.

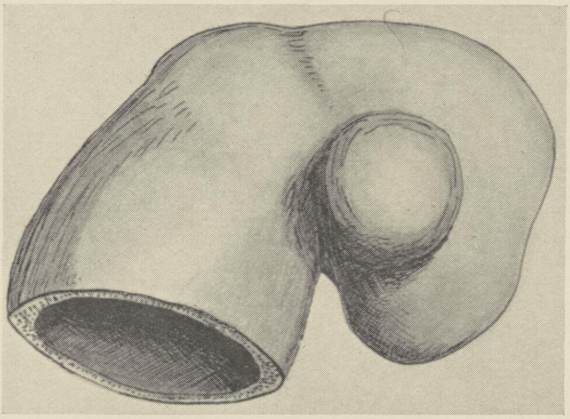


Fig. 18. Model of brain and optic vesicle of 4 mm. human embryo seen from the right side.

At this stage a change is apparent in that portion of the surface ectoderm which is in contact with the optic vesicle. The surface layer here thickens considerably so that one can now speak of a plate of thickened ectoderm in this region. This is the *lens plate.* This lens plate is slightly indented opposite the lower part of the optic vesicle. The small indentation is called the *fovea lentis* and is the first indication of the sinking of the plate which will form the *lens pit.*

At the same time one can perceive an alteration in the shape of the primary optic vesicle. This has now enlarged slightly, without corresponding increase in the width of its stalk, which thus appears to be relatively more constricted. The enlargement of the vesicle being greater in an upward than in a downward direction, the stalk also appears to be inserted more towards the bottom of the vesicle than previously. In addition to the increase in size of the upper part of the vesicle, there is a flattening of the lower and outer part

Digitized by Illinois College of Optometry Library

of it, namely, of that part which is in contact with the lens plate, and also of the region below this. This alteration in form can be seen in Fig. 19, which represents a front view of a model of half the fore-brain and the right optic vesicle of a 4·5 human embryo. A portion of the wall of the optic vesicle has been cut away so that one can see into its cavity. On looking at the cut edge of the ectoderm here it is apparent that differentiation is occurring. The portion of

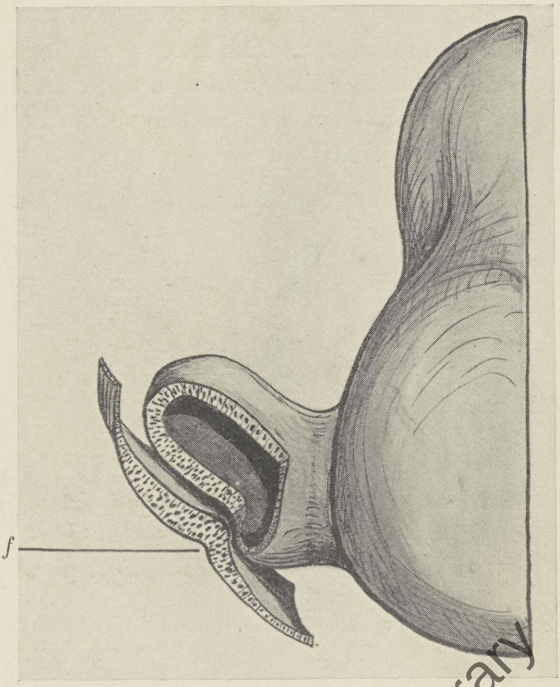


Fig. 19. Front view of model of half fore-brain and right optic vesicle of a 4·5 human embryo. The vesicle is cut open so that its cavity can be seen. The portion of the surface ectoderm in contact with the vesicle is represented, shewing the commencing *fovea lentis* (*f*).

the wall of the optic vesicle which is in contact with the lens plate is thickening, while the rest of the wall remains thin.

Microscopic sections of the wall of the vesicle shew that opposite the lens plate the nuclei are proliferating and are arranged in several rows, while the rest of the wall of the vesicle is only one cell thick. This difference becomes more apparent still during the course of development, the thickened portion specialising to form the layers of the retina from the nerve fibre layer to the rods and cones, while the rest of the wall of the vesicle remains thin and finally forms the pigment epithelium of the retina.

This stage (4·5 mm.) shews the beginning of an important phase

Digitized by Illinois College of Optometry Library

in the development of the eye, namely, the stage of **invagination of the primary optic vesicle.**

The object of the invagination is, by the indentation of the more superficial wall of the optic vesicle, to produce a *secondary optic vesicle* or **optic cup** the walls of which are formed by the approximation of the indented superficial wall to the deep one.

This flattening and the invagination which follows it occurs, as can be seen in Figs. 19 and 20, from below as well as from the outer

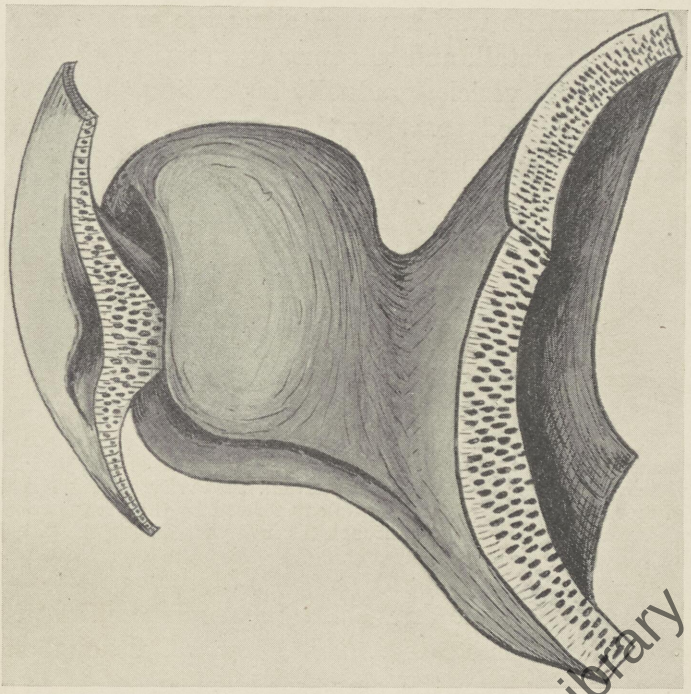


Fig. 20. Model of optic cup and lens thickening of a 5·5 human embryo shewing invagination of the optic vesicle to form the optic cup, and the deepening of the lens pit.

side, so that by the 5·5 mm. stage shewn in Fig. 20 a shallow groove has been formed running from the cup-like depression inwards along the lower aspect of the short and wide optic stalk almost on to the wall of the fore-brain. The margins of the invaginated area shew active growth at this stage and begin to form a definite rim around the depression, so that the presence of an optic cup can now be recognised.

The invagination rapidly progresses until the original outer wall of the optic vesicle becomes approximated to the inner wall (Fig. 21).

The optic cup is sometimes known as the secondary optic vesicle, but this term is better avoided owing to the possibility of confusion with the primary optic vesicle.

Digitized by Illinois College of Optometry Library

The cavity of the optic cup is occupied by the lens thickening, the small depression in the lower part of which has now deepened to form a more definite *lens pit*. The lental area, however, only occupies the optic cup proper, not the groove which runs from this along the lower part of the optic stalk. This groove is filled with mesoderm. It has been stated that the surface ectoderm of the lens plate and the neural ectoderm of the primary optic vesicle were in direct contact from the beginning, no mesoderm intervening. At this stage, however, the thin layer of paraxial mesoderm below the eye begins to find its way upwards along the groove in the lower aspect of the optic stalk and so comes to grow in between the lens plate and the optic vesicle, gradually separating the two. As they are, as it were, pushed apart by the entering mesoderm (which is definitely vaso-formative and soon gives rise to blood vessels), fine



Fig. 21. Scheme shewing the increasing apposition of the superficial and deep walls of the optic vesicle during the process of invagination. *A*, cavity of primary optic vesicle. *B*, cavity of secondary optic vesicle or optic cup formed by the invagination. The first three diagrams shew vertical sections through the invaginated area, the last gives a horizontal section.

strands of protoplasm are drawn out between them, between which the mesoderm cells penetrate, so that they are, although separated, still in direct continuity with each other by means of a fine reticulum of drawn-out protoplasmic adhesions. This fact is intimately connected with the development of the vitreous.

The groove involving the under side of the optic cup and stalk is known as the *foetal fissure*, the *foetal ocular cleft* or the *choroidal fissure*.

The last name is the oldest and the most frequently used, but it should if possible be abandoned as it tends to create the impression that the cleft has some connection with the choroid. It is true that at this early stage the cleft is filled with a vaso-formative mesoderm similar to that which encircles the eye and gives rise to its choroid coat, and in continuity with it, but this is its only connection. The vessel which enters the cleft becomes the hyaloid artery, a branch of the ophthalmic artery and quite distinct from its ciliary branches. The term "choroidal fissure" should therefore only be used if it is fully realised that the nomenclature refers solely to the vascularity of its mesoderm, the only quality common to it and the choroid proper. The term "foetal fissure" is preferable, and will be used here.

Digitized by Illinois College of Optometry Library

The process of invagination of the optic vesicle to form the optic cup has always aroused speculation. There are two main problems connected with it to be considered.

A. Is the pushing in of the outer face of the optic vesicle a mechanical result of the pressure of the lens pit on it, or is it a peculiarity of growth inherent in the vesicle itself, in which case the invagination of the lens pit might be secondary, seeing that they are adherent?

B. Why should the invagination occur from below as well as from the outer side, so that the optic stalk is also involved, though this is never in contact with the lens thickening?

(A) The first problem has been solved by means of experiments on the lower vertebrates, in the embryos of which operations of excision and transplantation can be performed without stopping the development of the embryo.

It can be shewn in frog embryos[1] that, if a primary optic vesicle be removed before invagination has begun and transplanted to some other part of the body where it is not in contact with surface ectoderm, invagination will occur and an optic cup be formed just the same. The cup so formed will not contain vitreous, and will not undergo complete cellular differentiation, but as regards its shape it will be at first normal.

Another experiment will shed further light on the subject. If an excised optic vesicle shewing no invagination be transplanted beneath the skin of the embryo in some other part of the body, or even beneath the skin of another embryo of the same or an allied species, the overlying ectoderm with which it is in contact will thicken and attempt to form a lens.

These two experiments shew:

1. That the power of invagination is inherent in the vesicle, a fact which might have been suspected since invagination normally affects not only that part of the vesicle which is in contact with the lens plate, but also the lower part of the stalk, where contact is with undifferentiated mesoderm only.

2. That the formation of the lens plate and its subsequent behaviour occur as a reaction on the part of the undifferentiated surface ectoderm to some stimulus received from contact with the invaginating vesicle, since this stimulus seems to be effective for surface ectoderm in any situation which is subjected to the contact.

That the lens can be regarded as a secondary modification which can be produced promiscuously in response to the need of the optic

[1] Lewis, Spemann.

Digitized by Illinois College of Optometry Library

vesicle, is also suggested by the experiments of other observers on *Rana sylvatica* and young salamanders, in which, after removal[1] of the lens from the eye, a new lens is regenerated from the neural ectoderm of the edge of the optic cup.

We may therefore say that the primal factor in the formation of the eye is the inherent power of the optic vesicle to invaginate. This leads us on to the second problem mentioned above, namely, the rationale of the formation of the foetal fissure.

(B) This fissure apparently occurs in all developing vertebrate eyes. It is definitely associated with the entrance of vascular meso-

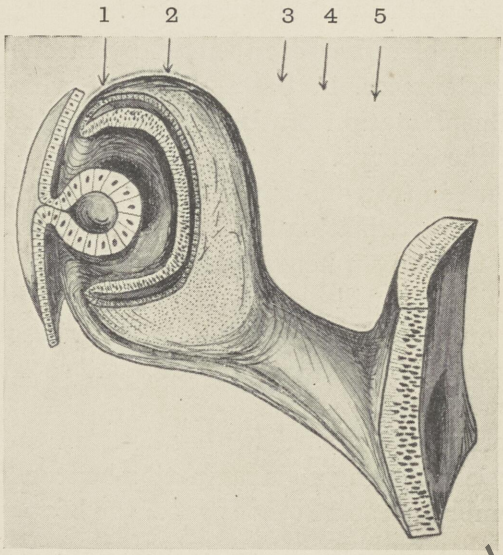


Fig. 22. Model of optic cup of 7·5 mm. human embryo. The wall of the cup has been cut away to shew the two layers. The lens vesicle has been opened to shew the cavity and the narrow passage running from this through the lens stalk. The arrows mark the situation of the sections seen in Fig. 23.

derm into the optic cup, but it is probably not primarily a mechanism to permit of this, since in large classes of vertebrates (birds and reptiles) the amount of mesoderm which enters the eye through the cleft is very small indeed and does not appear to play much part in intra-ocular nutrition. The probable reason for the presence of the cleft is suggested by the fact that it invariably involves the optic stalk.

If one considers the shape of the optic cup after invagination and before closure of the cleft, as shewn in Fig. 22 (7·5 mm. embryo) it becomes apparent that direct continuity has been established between the inner layer of the optic cup at the posterior pole of the

[1] Colucci, Wolff, Muller, Fischel.

Digitized by Illinois College of Optometry Library

eye, and the optic stalk. At the region of the insertion of the stalk, the inner layer of the cup passes directly into the inner layer of the stalk, so that the posterior pole of the eye, looked at from the front, shews the open cleft running upwards into a small funnel-shaped depression which marks the situation of insertion of the optic stalk. Fig. 23 makes this continuity clearer. It shews the appearance of sections of the eye in Fig. 22 at the positions indicated by the arrows. The connection between the inner layer of cup and of stalk is obvious. Even after the cleft has closed, continuity is maintained at this upper end, so that when the nerve fibres begin to grow from the

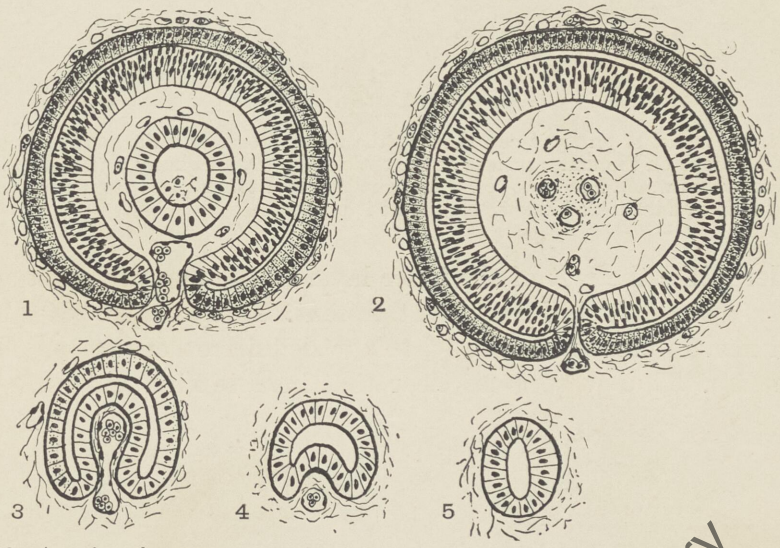


Fig. 23. A series of transverse sections through the optic cup and stalk of the eye seen in Fig. 22. The sections pass through the planes indicated by the arrows in Fig. 22.

ganglion cells, which are developed from the inner layer of the cup, their path is open and direct from the inner layer to the centre of the optic stalk and so back to the brain. If invagination of the cup had occurred symmetrically from its outer side, without formation of a cleft, there would have been no direct continuity between the inner (retinal) layer and the stalk, so that nerve fibres developing on the inner surface of the cup would have had no direct path back to the brain. A glance at Figs. 24 and 25 will make this quite clear. In both these diagrams *A* represents the real state of affairs, *B* the condition which would result if no foetal fissure were formed. One can easily see how, in Fig. 25 *A*, nerve fibres can grow directly from the inner layer into the stalk, which then becomes the optic nerve.

Digitized by Illinois College of Optometry Library

By 7·5 mm., then, one can recognise the place where the nerve fibres will subsequently leave the eye, that is to say, the optic disc or nerve head, but inasmuch as there are no nerve fibres yet and the site of the optic disc is simply formed of (undifferentiated) neural

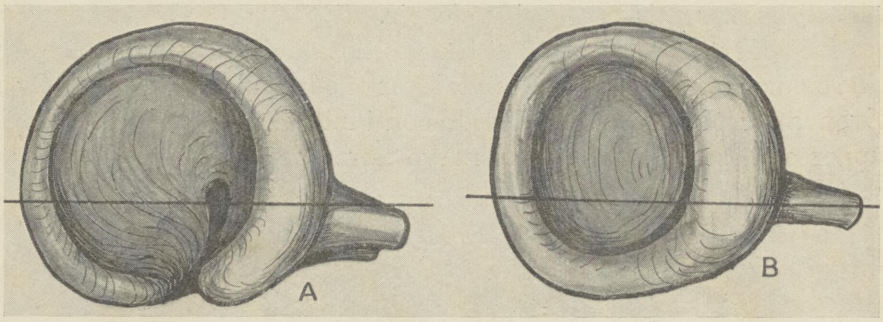


Fig. 24. *A*, model of an optic cup shewing the foetal fissure and the continuity of this with the groove on the under surface of the optic stalk. *B*, imaginary model shewing the condition which would have resulted if invagination had taken place from outside only, instead of from outside and below. No fissure is present.

ectoderm like the rest of the inner layer of the cup, we must speak of a *primitive epithelial papilla*[1] at present. This will give place later, when nerve fibres grow into it, to the definitive nervous papilla or optic disc. Thus it becomes clear that invagination and formation

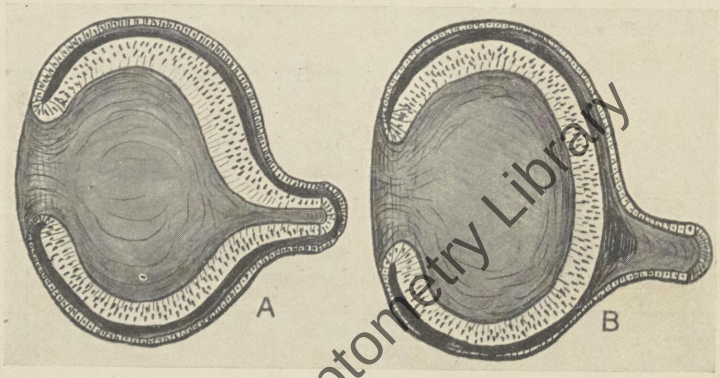


Fig. 25. *A* and *B* represent sections (at the level indicated by the lines in Fig. 24) of *A* and *B* in Fig. 24.

of the foetal cleft is an inherent property of the vesicle existing to ensure the provision of a clear path from the inner (nerve-fibre-bearing) layer of the optic cup to the brain via the primitive epithelial papilla and inner layer of the optic stalk.

[1] *Papilla nervi optici primitiva seu epithelialis* of von Szily.

Digitized by Illinois College of Optometry Library

The 7·5 mm. stage shewn in Fig. 22 requires further description. Dealing first with the optic cup, a portion of the wall of this has been cut away so as to shew how it consists of two layers. These two layers are the front and back walls of the primary optic vesicle which have come together owing to the invagination. There is still a space between them, which is the remains of the cavity of the primary optic vesicle and is of course continuous through the cavity of the optic stalk with the cavity of the fore-brain, so that the eye is still quite obviously an outlying process of the central nervous system. Owing to the invagination having involved the stalk also, this is now crescentic in cross-section, not circular.

The stalk has elongated since the 5·5 mm. stage, and the eye is farther from the brain. The cup has deepened and the margins of the foetal fissure are growing rapidly so that the lower part of the eye is coming into being, though the upper part is still much the larger (Figs. 11, 19, 20, 22).

The surface ectoderm has also undergone an important change. The lens pit has deepened without corresponding widening of its external opening, so that by a process of invagination a *lens vesicle* has been formed. This is a small spherical body, having a central cavity connected at first with the exterior by a fine channel in the *lens stalk* (i.e. the cells by which the lens vesicle is still attached to the surface ectoderm). This channel is seen in Fig. 22, but it soon becomes obliterated, the lens stalk constricts and the vesicle becomes entirely separated from the surface ectoderm; mesoderm rapidly grows up between the two, and no trace of its site of attachment to the surface remains.

Congenital Abnormalities

Certain congenital abnormalities of the eye may have their origin in aberrations of development which arise at or before this stage.

In considering the mechanism of the production of congenital abnormalities of any organ, one has to bear in mind certain possibilities. The simplest thing that may happen is arrest of development at some stage which is normally transient. Then the resulting abnormality will resemble a condition which is normal at an earlier age and the period at which the disturbance of growth occurred can be determined. It is seldom, however, that the matter is as straightforward as this. Usually the (resulting) abnormality does not resemble any normal stage. Such conditions must be looked on as pure aberrations of growth not to be satisfactorily explained by any amount of study of purely normal embryos, although from a study of what structures are or are not present in the abnormal individual one can often form some idea of the stage of development at which the aberration occurred. The exact mechanism of its production must necessarily be a mystery, since we know practically

Digitized by Illinois College of Optometry Library

nothing of the forces which govern the interactions of growing tissues in normal embryos.

Occasionally an anomaly arises which, while abnormal in that particular individual, resembles a condition normally present in some other species. In these cases some stage of development common to both the species may be found, at which stage the anomaly may have arisen. Such phenomena may be loosely spoken of as "phylogenetic memories" or atavism, but very little value can be attached to them as evidences of relationship or as explanations of congenital deformities, unless the ontogenetic processes include the assumed phylogeny.

A large number of the slighter congenital anomalies of the eye can be partially explained in a different way by saying that they are evidences of the pluripotentiality of embryonic cells. Thus if one considers a cell of the wall of the primary optic vesicle, it is apparent that, since from the primary optic vesicle are formed the retina, the uveal pigment, the intrinsic muscles of the iris and the optic nerve, each cell of the primary vesicle might conceivably contain the potentiality of developing either into a nerve cell, a pigment producing cell, a muscle cell or a neuroglial cell. Which it will develop into appears to be determined in some way by its position, but it occasionally happens that the determining influence is not sufficiently strong and an aberration appears which is quite obviously due to the differentiation of a cell or cells into a tissue which they should not in that position normally form[1], but the potentiality of forming which they contain. This will account for the occasional presence of retinal elements or pigment cells in the optic nerve, or of pigment epithelium in the inner layer of the optic cup.

The question arises as to what congenital abnormalities might result if growth were interfered with at or before this 7·5 mm. stage.

In the first place there might be a total failure of one or both primary optic vesicles to bud out from the fore-brain. This would result in a condition of *true anophthalmia*, no trace of the ectodermal structures of the eye being formed at all, though there might be differentiation of mesoderm so that an orbit was present. This abnormality, though known to occur, is extremely rare, since an aberration of growth gross enough to produce complete suppression of the front of the fore-brain occurring at this early stage is liable to end in the production of an embryo too abnormal to survive at all. Clinically the condition is almost impossible to distinguish from severe degrees of microphthalmia, in which the eye can only be demonstrated by removal and sectioning of the contents of the orbit.

Secondly, if the primary optic vesicle failed to invaginate successfully its cavity might undergo cystic dilatation and the condition known as *congenitally cystic eye-ball* would result. In this condition the orbit contains, instead of an eye, a large cyst, in the walls of which are traces of nervous elements, the tissue in the anterior part of the cyst resembling retina, that posteriorly being pigmented. Here the arrest of development has occurred very early and very

[1] Coats.

Digitized by Illinois College of Optometry Library

imperfect differentiation of the neural ectoderm has taken place and the cavity of the cyst is the cavity of the primary optic vesicle. If, however, the arrest of development occurred a little later, after invagination of the primary vesicle, but before closure of the foetal fissure, then a lens vesicle would have been formed and a certain amount of differentiation of the walls of the optic cup would be present, but the eye would be very small (microphthalmia) and the cleft would be open (coloboma of retina). In such microphthalmic eyes there is apparently often a tendency for irregular over-growth of the layers of the optic cup in the region of the open fissure, so that cysts are formed behind and below the eye. Some of these cysts are lined with partially differentiated retina and pigment epithelium and their cavities are in communication with the cavity of the optic cup. They must be carefully distinguished from the cysts

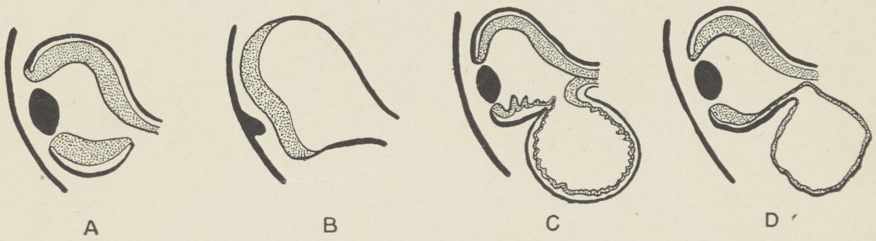


Fig. 26. Diagrammatic representation of *A*, normal optic cup; *B*, congenitally cystic eye; *C*, microphthalmia with orbital cysts of optic cup; and *D*, microphthalmia with cystic dilatation of primary optic vesicle in the fissural region.

of the congenitally cystic eye described above, in which the cavity of the cyst is the cavity of the primary optic vesicle and no microphthalmic eye is present[1] (Fig. 26 will make this distinction clear). Cysts in connection with microphthalmic eyes may also be formed by dilatation of a localised portion of the cavity of the primary optic vesicle in the fissural region. In this case they are lined by a single layer of poorly differentiated neural ectoderm.

Abnormalities of the lens vesicle might arise at this stage. Clinical examples of congenital aphakia (complete failure of a lens vesicle to form from the surface ectoderm) are practically unknown, unless in association with some other gross abnormality such as congenital cystic eye or an extreme grade of microphthalmia. In most so-called cases of congenital aphakia, microscopic examination has revealed traces of a lens. The capsule is usually present and there is other evidence to shew that the lens had really been formed but had subsequently degenerated and been absorbed.

[1] Collins and Mayou.

Digitized by Illinois College of Optometry Library

A case has however been recorded of a 10 mm. human embryo in which, though the optic cup had invaginated normally and the eye was of good shape and size for the stage of development, a lens thickening only was present on the surface ectoderm and no pit or lens vesicle had been formed at all[1]. This embryo is interesting both in that it shews that failure of the lens vesicle can occur apart from failure of invagination of the primary optic vesicle, and also that it adduces further proof, if this were needed, that invagination of the cup is not dependent on the presence of the lens vesicle.

If the lens vesicle were not absent entirely, its separation from the surface ectoderm might be delayed, giving rise to some abnormality of the anterior pole, e.g. anterior lenticonus or anterior polar cataract.

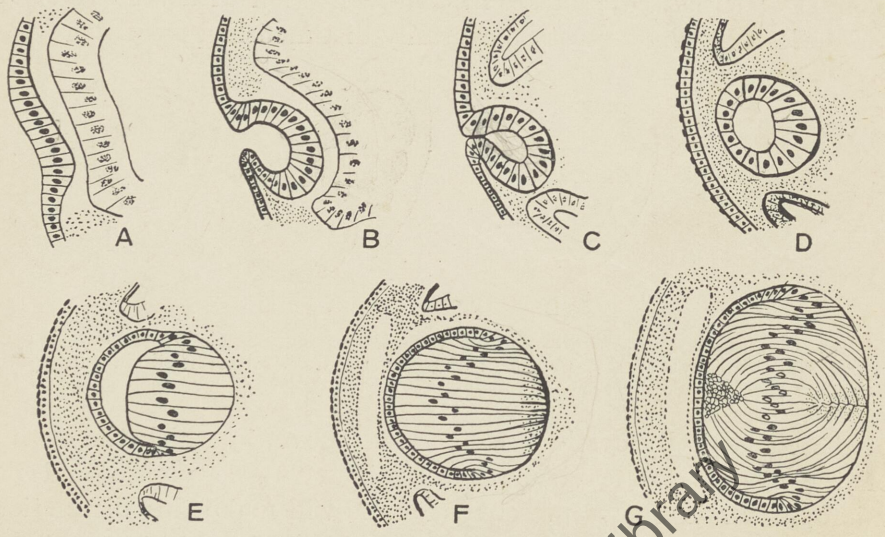


Fig. 27. Scheme to shew the development of the lens. *A*, lens thickening. *B*, lens pit. *C*, lens pit closing. *D*, lens vesicle. *E*, elongation of cells of posterior wall of lens vesicle. *F*, obliteration of cavity of lens vesicle by cells of posterior wall. *G*, formation of lens sutures by the meeting of the fibres developed in the equatorial region.

Formation of the Lens

The further growth of the lens vesicle can now be considered separately. Fig. 27 shews the general line of development which it follows.

It has separated from the surface ectoderm by the 10 mm. stage and has the form of a hollow sphere. Almost immediately after its separation, the cells of its posterior wall elongate and encroach on the cavity of the sphere, which now becomes crescentic on section (Fig. 27, *D* and *E*). It is further filled by the elongating cells of the

[1] Mann.

Digitized by Illinois College of Optometry Library

posterior wall, which can now be recognised as early lens fibres. These soon completely fill it and all that remains by the 16 mm. stage is a potential crescentic chink between the anterior ends of the cells of the posterior wall and the cells of the anterior wall, which have retained their character of cubical epithelium. Fresh lens fibres are then formed from cells in the equatorial region, and these growing anteriorly and posteriorly towards the poles of the lens, meet the ends of their fellows in front of, and behind, the first formed lens fibres and so form the sutures of the lens. The sutures begin to appear about the beginning of the 3rd month (i.e. about 30 mm.).

The Closure of the Foetal Fissure and the Further Differentiation of the Optic Cup

Soon after the 10 mm. stage, the opposed margins of the foetal fissure begin to come together. They meet first in the central portion of the fissure and fuse here, fusion spreading up and down the fissure until, by the 13 mm. stage, only the two extremities of the fissure remain open, the upper one allowing of the passage of the mesoderm around the hyaloid artery into the interior of the cup, the lower one appearing as a notch at the pupillary margin. Soon after this stage this notch disappears completely. The portion of the fissure involving the optic stalk disappears more gradually, as will be explained later. Fig. 28 shews the optic cup of a 13 mm. human embryo. A portion of its wall has been removed so that the two layers composing it can be seen. The inner or retinal layer is thick and beginning to differentiate; the outer or pigment layer is only one cell thick. The space between the two layers is all that remains of the cavity of the primary optic vesicle. This space remains open for a long time and even in adult life the cohesion of the two layers is very slight, the retina always tending to separate from its pigment layer on fixation or dissection, and indeed under pathological conditions also.

The most marked change which has occurred in the external form of the eye is that due to the growth of the lower part of the cup, namely those areas bounding the foetal fissure. This growth has made the part of the cup below the insertion of the optic stalk as large as the part above, so that the optic stalk now is inserted into the middle of the posterior pole of the eye, not into its lower portion as appeared in Figs. 19, 20 and 22. At the same time the foetal fissure has closed except for (*a*) a small gap or notch at the margin of the cup which marks its anterior (or lower) end, and (*b*) a small hole at its extreme upper end where the hyaloid artery enters the

Digitized by Illinois College of Optometry Library

cup in the centre of the primitive epithelial papilla. There is also for a short time a small remnant of the fissure on the stalk. This shews as a groove on the under surface of the optic stalk in the region where the vascular mesoderm of the hyaloid artery enters it. The stalk is shewn in cross-section in the diagram. An inner and an outer layer can be recognised, as in the optic cup, with the cavity of the primary optic vesicle between them. As in the cup, the two layers have different fates, the inner one being invaded by fibres growing from the ganglion cell layer of the developing retina, until the cells are unrecognisable for the mass of fibres, the outer one (which does not

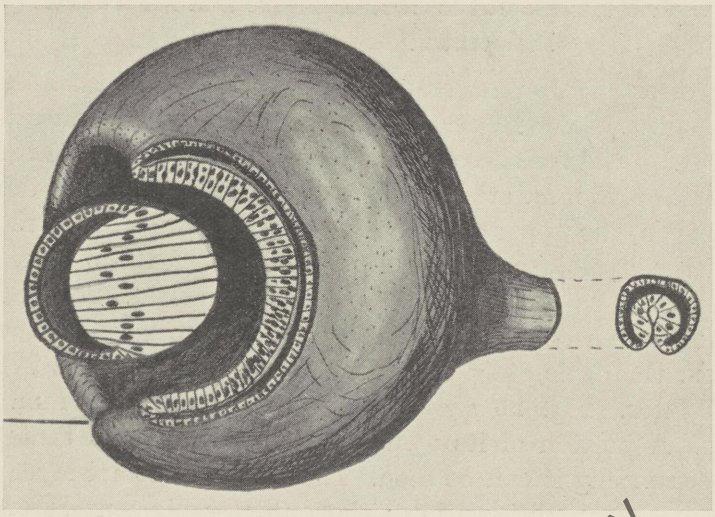


Fig. 28. Model of the optic cup of a 13 mm. human embryo. A portion of the lateral wall of the cup and of the lens vesicle has been cut away. *n* points to notch in margin at site of fissure. The stalk is shewn in cross-section on the right of the figure.

develop pigment in man) becoming converted into the neuroglial supporting tissue of the optic nerve. The optic stalk is elongating and thinning, and now resembles, in relative size at least, the optic nerve.

At this stage (13 mm.) the margin of the optic cup does not reach beyond the equator of the lens, and is entirely undifferentiated. There is therefore no sign of the ectodermal portion of the iris and ciliary body. These structures appear relatively late, the first sign of active growth of the margin of the cup being about 50 mm. Up to this time the eye has increased as a whole, all trace of the foetal fissure has disappeared (except of course the passage for the hyaloid artery into the interior of the optic stalk and thence into the eye) and growth has mainly been in the direction of elaboration of the

Digitized by Illinois College of Optometry Library

intra-ocular blood supply (dealt with below) and increasing differentiation of the layers of the retina.

At 50 mm. (3rd month) active growth begins at the margin of the cup and leads to the appearance of folds just behind the growing edge, in the situation of the future ciliary processes. These folds increase in size and number, and the growing margin in front of them extends towards the front of the lens as a double layer of epithelium (the outer layer alone pigmented) to form the ectodermal part of



Fig. 29. Horizontal section of a model of the eye of a 15 mm. human embryo. The proximal branches of the hyaloid artery are shewn cut. The vascular capsule of the lens is not shewn.

the iris (the posterior pigmented layers). This "ectodermal iris" begins about 65 mm. (latter part of 3rd month) and can be seen in Fig. 29 as a small blunt margin just anterior to the folds of the primitive ciliary processes. It then grows steadily forwards over the anterior surface of the lens, so that by 8 months it is practically complete and the pupil fully formed and of the definitive size. At 4 months, however, a specialisation begins to appear on the anterior surface of the growing ectodermal iris at its free margin. A mass of unpigmented cells buds off from it here and differentiates to form

Digitized by Illinois College of Optometry Library

the sphincter and dilatator muscles of the iris, which are therefore developed directly from neural ectoderm.

The exact manner of this differentiation will be dealt with in Section IV. It is sufficient at present to realise that these muscles form an important exception to the general rule that muscles arise from mesoderm. The only other muscles of the human body which are at present known to arise from ectoderm are the arrectores pilorum of the skin, and these come from surface ectoderm, not neural ectoderm.

Thus we see how the pigment epithelium of the ciliary processes and of the posterior layers of the iris is developed by a forward growth of the margin of the optic cup which only begins some time after closure of the foetal fissure. It is important to realise this, for from time to time the hypothetical open end of the fissure has been called in to explain the existence of congenital clefts which involve the iris only. Any cleft due to persistence of the fissure will involve the ciliary body as well and also probably the *pars plana* of the retina, since everything in front of this appears after the fissure has normally ceased to exist. It is also well known that clefts involving the iris only (coloboma iridis) may occur in any position, and, what is more important, may be multiple. It seems probable therefore that some other cause is at work in their production, and to understand them one must consider the development of the associated mesoderm as well. This probably plays some part, by persistence or undue toughness, in hindering the proper growth of the very thin ectodermal edge of the cup which should form the iris.

The Associated Mesoderm

The mesoderm in association with the primary optic vesicle is at first (3–4 mm. stage) almost entirely undifferentiated. It forms a loose mesh-work of stellate cells connected by interlacing processes, and no such tissues as cartilage, muscle or fibrous tissue can be made out. The only differentiation present is that of the blood cells. Nucleated erythrocytes can be easily recognised and can be seen to lie in spaces in the mesodermal mesh-work which are lined by a definite wall formed of a single layer of flattened mesoderm cells (endothelium). We can therefore distinguish two types of mesoderm at this stage, vascular and stromal. The stromal mesoderm in the neighbourhood of the optic vesicle can be recognised as belonging to the two main mesodermal masses (see p. 16), i.e. paraxial mesoderm, immediately surrounding the optic vesicle and in contact with it (except where it is in direct contact with the surface ectoderm), and visceral (maxillary) mesoderm, lying below this.

Digitized by Illinois College of Optometry Library

Both types of mesoderm are vascularised. They are similar in appearance, but slight differences of texture and a faint line of vascular condensation where they lie in contact, serve to distinguish them (Fig. 30).

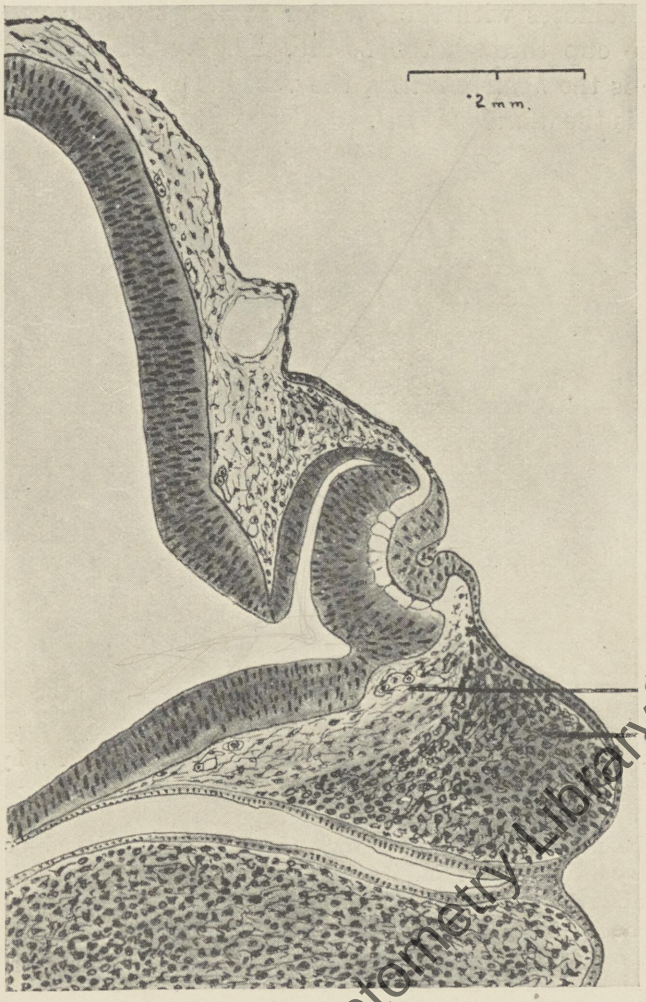


Fig. 30. Transverse section through the optic vesicle and maxillary process of a 5 mm. human embryo. *a*, visceral mesoderm of maxillary process; *b*, paraxial mesoderm.

The differentiation about to be described involves the paraxial mesoderm only.

At the 4·5 mm. stage the distribution of the blood vessels can be made out, though it is only possible to distinguish arteries from veins by their position, there being no difference in their structure. The region of greatest vascularity is at the lower part of the optic cup

Digitized by Illinois College of Optometry Library

in the region of the foetal fissure. Here are two sets of vessels, which anastomose freely, one set passing into the interior of the cup along the fissure, the other growing upwards on either side of this along the margins of the cup (Fig. 31). This last group of vessels soon forms a complete vascular ring around the margin of the cup, which anastomoses with the anterior branches of the vessel which entered the cup through the fissure. The vessel entering through the fissure is the *hyaloid artery*, the vascular ring round the margin of the cup is the *annular vessel*.

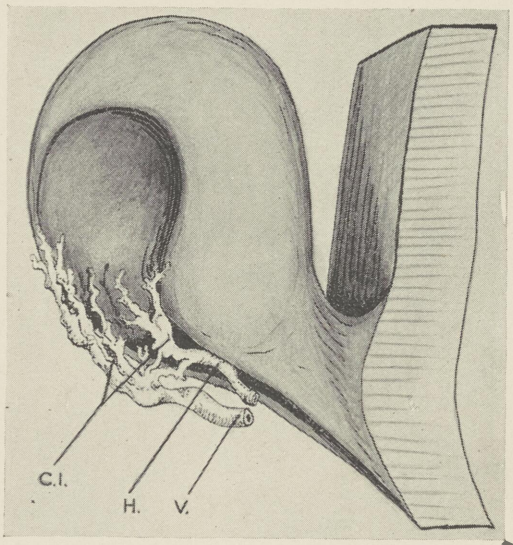


Fig. 31. Model of the optic cup of a 5 mm. human embryo, shewing the developing blood vessels. *C.I.*, branches vascularising the margins of the optic cup; *H.*, hyaloid artery entering the foetal fissure; *V.*, main vessel supplying eye from below.

This has been named the *annular artery* by Fuchs, but since blood from the hyaloid artery drains into it and it itself anastomoses freely with the choroidal veins, it is doubtful whether it should be looked on as arterial or venous. It is therefore better to call it the annular vessel. At this stage, when there is no differentiation of the walls of the vessels and all the vessels have the appearance of dilated thin-walled capillaries, it is unprofitable to attempt to explain the embryonic circulation by an appeal to the stereotyped arrangement of artery → arteriole → capillary plexus → venule → vein, found in the adult. In many places arteries appear to run directly into veins without the intervention of any capillary net or else are connected by large vessels (like the annular vessel) which cannot be classed either as arteries or veins. Moreover, even in the adult eye, the arrangement of direct arterio-venous anastomosis is retained to a striking degree by the vessels of the iris. It is probable that in these early embryos the direction of the blood flow, in any one of the innumerable thin-walled vessels which form the blood supply of the developing eye, is not constant from minute to minute, any more than it is in the capillary arcades at the limbus of the cornea of the adult eye. If the circulation here is observed

Digitized by Illinois College of Optometry Library

with slit-lamp and binocular microscope, and one particular capillary loop watched carefully, one will see the blood flowing steadily for a few seconds, the stream will then slow down, the vessel may become completely empty for a time or a sort of swaying motion may be observed in its contents and then the blood flow will be re-established just as briskly in the opposite direction. This gives some idea of the probable state of affairs in the rich mesh of vessels of a young embryo.

The hyaloid artery breaks up into branches and forms the *foetal intra-ocular blood system*. This consists, broadly speaking, of two sets of vessels, the first forming a net-work on the posterior surface of the lens and draining forwards round the equator of this into the



Fig. 32. Diagrammatic representation of the intra- and extra-ocular blood systems at 25 mm. stage. *a*, annular vessel; *b*, choroidal vessel; *c*, hyaloid artery.

annular vessel, and the second ramifying in the vitreous and anastomosing anteriorly with the first set. The first set forms part of the vascular capsule of the lens (*tunica vasculosa lentis*) and the vessels of the second set are known as the *vasa hyaloidea propria*.

Very soon after the 10 mm. stage the vascular arrangements of the embryonic eye can be divided into (*a*) the extra-ocular blood system, which includes the vessels of the orbit and of the primitive choroid, and (*b*) the intra-ocular system, which consists of the hyaloid artery and its branches and the resulting vascular capsule of the lens.

The extra-ocular blood system forms the rudiment of the definitive extra-ocular blood supply, and, with certain modifications, persists. The intra-ocular blood supply (derived from the hyaloid), on the other hand, atrophies entirely, and a new and definitive intra-ocular system (*arteria et vena centrales retinae*) is formed at a later stage.

Digitized by Illinois College of Optometry Library

Fig. 32 shews a diagrammatic representation of the two blood systems at about the 25 mm. stage.

Associated with the formation of the foetal blood supply is the appearance of the anterior chamber and the differentiation of the *substantia propria* of the cornea and the mesodermal stroma of the iris. This occurs at 18–20 mm., long before the ectodermal portion of the iris has begun to extend out from the margin of the optic cup. Fig. 33 will help to explain the formation of the anterior chamber.

After the separation of the lens vesicle from the surface ectoderm, described on p. 30, the surrounding mesoderm grows in and fills

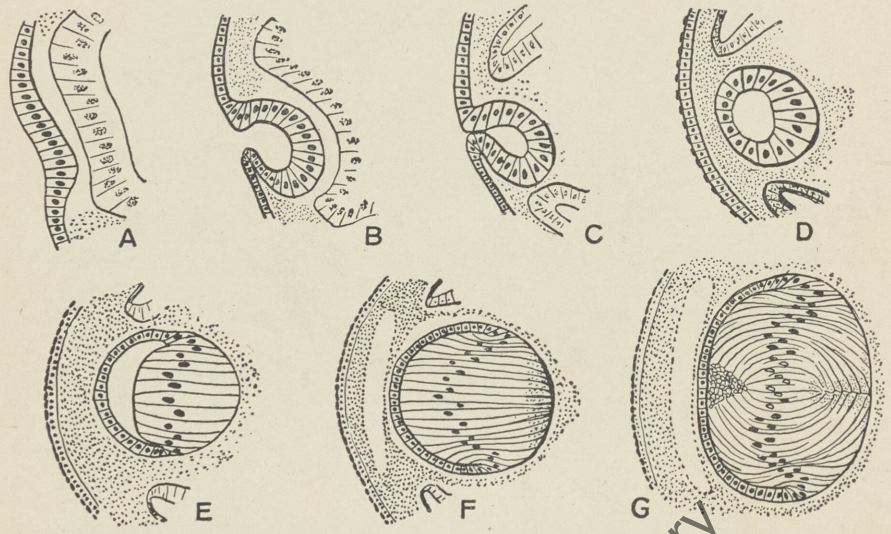


Fig. 33. Diagrams to shew the formation of the anterior chamber. In *F* the mesoderm lying between the lens and the surface ectoderm has split into two layers, leaving a closed space—the anterior chamber—between them.

the space between the lens and the surface. This mesoderm is continuous round the lens with that in the interior of the optic cup. At or before the 18 mm. stage vacuoles begin to form in this mesoderm, which, coalescing, lead to a split occurring which separates the mesoderm between the lens and surface ectoderm into two layers. Of these, the superficial one is the thicker and, remaining in contact with the surface ectoderm, subsequently develops into the *substantia propria* of the cornea. The deeper (and thinner) one remains in contact with the anterior surface of the lens. Its central portion finally disappears (being that part of the anterior vascular capsule which atrophies during the 7–8th month) while its peripheral portion, which is from the beginning thicker, remains as the superficial layer of the iris stroma peripheral to the lesser circle.

Digitized by Illinois College of Optometry Library

The mesoderm associated with the posterior part of the eye very early shews a hollow cone of condensation, having its apex at the back of the orbit around the optic stalk. This tent-like arrangement soon begins to segment into four main portions which represent the rudiments of the *extrinsic eye muscles*. These eye muscles can be recognised as separate at an early period (about 7–8 mm.).

The *sclerotic* arises as a thin sheet of condensation outside the primitive choroid. It is thickest at first in the neighbourhood of the insertions of the extrinsic eye muscles. A certain amount of loose cellular mesoderm is included within it and lies between the sclerotic condensation and the ectoderm of the optic cup. This forms the *stroma of the choroid*, and the lamina suprachoroidea. The capillaries of the chorio-capillaris can be recognised very early (7 mm.). More anteriorly, after 48 mm. (when the margin of the cup begins to shew ridges and grooves) the mesoderm condenses to form the *ciliary muscle* and the *mesodermal cores* of the *ciliary processes*. Fig. 34 shews a section through the orbit of a 3 months foetus. The ciliary muscle, in contra-distinction to the other intrinsic eye muscles (the sphincter and dilatator pupillae) is developed from paraxial mesoderm like the extrinsic muscles.

The choroidal net seems to develop wherever mesoderm is in contact with pigmented epithelium. It appears *pari passû* with the pigment and appears to be in some way related to this, in that if for any reason pigment is absent over an area of the surface of the optic cup, the choroid is absent also. This is seen in those cases of coloboma of the choroid in which the intercalary membrane of the floor of the coloboma resembles the inner layer of the optic cup, and is not pigmented. It also occurs over a certain area below the nerve in birds, which is normally unpigmented and over which choroid does not develop. Whether the presence of pigment is determined by the development of the choroid or *vice versa* is not definitely proven, as they seem to appear almost simultaneously.

It has occasionally been stated that the cornea, lens and other transparent tissues of the eye are at first opaque and undergo a process of clearing during development. This is a fallacy based on the appearance of young embryos after fixation in alcohol. If a young embryo, for example, a four-days-old chick, be examined when perfectly fresh (i.e. still alive, the heart still beating) it appears quite transparent, like clear glass, and the surface outline is difficult to see. The only tissues which are opaque, and therefore shew distinctly, are the blood cells and the pigment epithelium of the eye. The form of the eye shews up plainly but only by virtue of the pigment, the other structures being perfectly transparent like the rest of the body of the embryo. This applies also to human (mammalian) embryos, but

Digitized by Illinois College of Optometry Library

is of course more difficult to verify as it is comparatively rarely that one has an opportunity of examining them fresh. The whole of the body becomes opaque and white either on the natural death of the embryo or on fixation in a protein coagulant such as alcohol or Zenker's fluid. As growth proceeds and the mesoderm begins to differentiate into primitive cartilage, muscle and connective tissue,

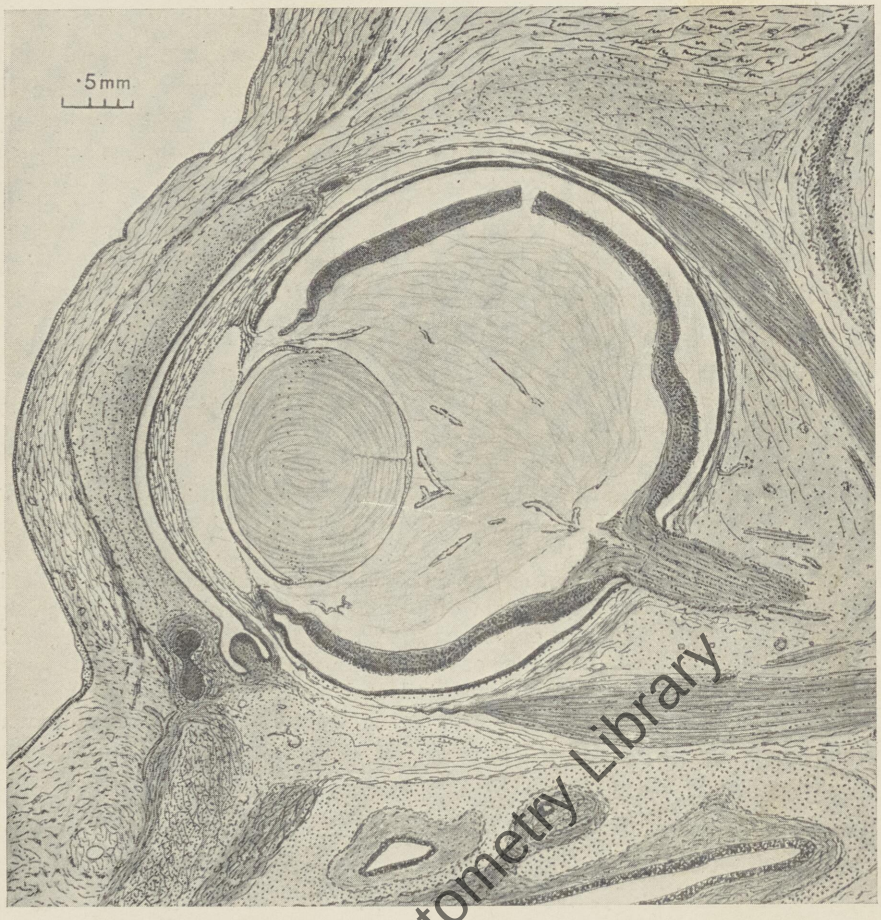


Fig. 34. Section through the eye and orbit of a 3 months foetus.

the indices of refraction of these various tissues come to differ from each other, the embryonic body is no longer so nearly homogeneous and light no longer passes unhindered through it. The cornea, lens and vitreous, however, retain their embryonic quality of transparency throughout life, so that one should rather speak of a process of opacification of all the other tissues than of clearing of these transparent ones during development.

Digitized by Illinois College of Optometry Library

The Eye at Birth

A study of the development of the eye must not end with the birth of the foetus. The eye of the new born does not in every particular resemble that of the adult, so that one must consider that development, though excessively retarded, continues throughout the whole of life.

Fig. 35 is a diagrammatic representation of the differences in shape (the two eyes being enlarged to approximately the same size) between the eye of a new born full-term foetus and an adult.

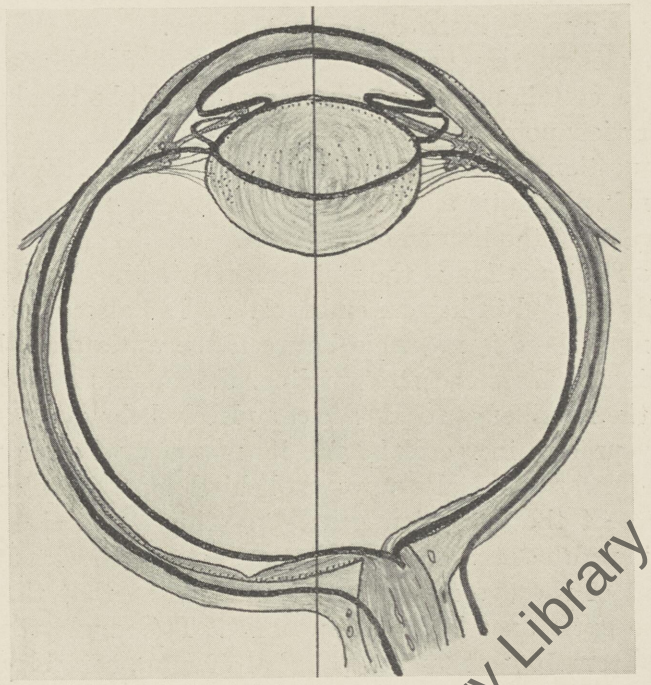


Fig. 35. Diagram (after Keibel and Mall) shewing the eye at birth (shaded) and the adult eye (black lines) both enlarged to the same size. Note the differences in shape of the lens and anterior chamber.

Certain differences are at once apparent, and it is obvious that these are most marked in the anterior half of the globe. In the new-born the *lens* is much more nearly spherical and appears relatively further back. Growth of the lens equatorially continues through life, but is not accompanied by increase in antero-posterior measurement, since the central fibres become compressed. The *angle* of the *anterior chamber* is wider and its lateral part looks much deeper, the central part of the iris appearing pushed forward by the lens. The ciliary processes are smaller than in the adult. At birth a line passing

Digitized by Illinois College of Optometry Library

through the centre of the cornea and lens will strike the retina at a point between the fovea and the optic disc, the medial half of the eye being slightly less well developed than the lateral. As growth proceeds this inequality disappears and the optic axis is displaced laterally until it reaches the fovea.

At birth the fibres of the optic nerve are partially myelinated. Myelination is complete about the 10th week after birth. In those animals whose eyes are not open at birth, Held has shewn that the stimulus of light hastens the myelination. The increase in size and weight of the eye through life runs parallel with that of the central nervous system, being roughly $3\frac{1}{2}$ times what it is at birth, while the body as a whole increases about 21 times.

Before closing this general survey of the development of the human eye, certain aspects of the subject should be touched on from a broader view point.

Two questions remain to be dealt with: first, the ontogenetic alteration in the optic axes, and second, the phylogenetic or evolutionary value of the human eye.

1. The first question is the simpler since the mechanism of it can be directly studied in human embryos. As has already been stated, up to 7 mm. there is no angle between the optic axes, both optic stalks lying in the same straight line. At the same stage one can see that the maxillary process lies completely below the eye. As the maxillary process increases in size its mesoderm begins to extend, not only forwards but also upwards behind the eye, between it and the region of the Gasserian ganglion. This is associated with an increase in width of the skull base in this region, and with a secondary movement of the eye forwards and inwards so that the angle between the optic axes becomes apparent. This angle then steadily decreases from 160° at 9 mm. to 72° at 40 mm., coincident with the further growth of a solid wedge of maxillary mesoderm upwards behind the eye, where it condenses to form the ali-sphenoid and pterygoid regions (see Section VII for sections and further details of the process).

The significance of this swinging round of the eyes during ontogenetic development can only be appreciated by considering the second question referred to above, namely the evolutionary value of the human eye.

2. In the first place one must deal with the relationship of the increase in size and importance of the maxillary process to the alteration of the optic axes, phylogenetically considered.

Among the Mammalia, the first definite displacement of the eyes

Digitized by Illinois College of Optometry Library

from their primitive position at the sides of the head appears in the Carnivora, in which the eyes look straight forward and the fields of vision overlap. This is also correlated with increased size of the maxillary process, but is not necessarily caused by it. In animals lower in the scale than the mammals, the ali-sphenoid region of the skull base is formed in paraxial mesoderm, not maxillary, and in consequence, the base of the skull is narrow and the 5th nerve passes through a foramen which appears to be situated on the side of the skull a great deal more laterally than it is in man and the anthropoids. In most of these animals the eyes are laterally placed and the fields of vision do not overlap. In some, however, a change has taken place in the optic axes, though the ali-sphenoid is still formed in paraxial mesoderm. This is the case in certain of the birds (notably owls) in which the eyes look more forward and there is the possibility of a certain amount of binocular vision in spite of the extreme narrowness of the base of the skull and brain.

Birds, are not on the direct evolutionary line. They are a very specialised off-shoot from a common sauropsidan stock possessing neither binocular vision nor wide skull base, but they are important in that they prove that binocular vision and forward movement of the eyes can arise as a specialisation quite apart from increased upward development of the back of the maxillary process, and indeed do appear considerably earlier in phylogeny.

The maxillary development is itself a secondary adaptation correlated with increase in the transverse size of the brain. This increase is most apparent in the width of the base of the brain, which, as it were, overlaps and becomes too wide for the narrow strip of paraxial mesoderm which previously supported it. A fresh shelf of supporting tissue has to be developed laterally and this is most easily achieved by the addition of more visceral mesoderm below the paraxial skull base, hence a "maxillary" ali-sphenoid.

The 5th nerve still leaves the skull at the outer edge of the paraxial shelf, but this is now some distance from the actual edge of the skull base, as is quite apparent in looking at any anthropoid skull. Coincidentally with this widening of the brain in mammals, we have a decreasing angle between the optic axes and the possibility of binocular vision, which in its turn leads to increased power of perception and hence leaves the way open for still further development of the brain. The development of the maxillary process and the swinging round of the eyes in the higher mammals may both be regarded as correlates of the increasing size and complexity of the central nervous system. It is probably incorrect to state either that

Digitized by Illinois College of Optometry Library

the maxillary process "pushes round" the eyes, or that the acquisition of binocular vision led in the first place to increase in size of the brain, since, as we have seen in birds, binocular vision may exist without either a large maxillary process or a large brain. The secret of the rise of the Anthropoid is in the complexity of the central appreciative mechanism rather than in the perfection of the peripheral receptive apparatus.

It has often been suggested that during development, in addition to this swinging round of the eyes to the front of the head, each globe underwent co-incidentally a rotation around the long axis of its stalk. This was said to be through an angle of 90° (Vossius). The reasons for postulating this rotation were:

1. The point of entry of the arteria centralis retinae into the optic stalk is at first directly below, and later on the outer side.
2. The superior rectus muscle is at first lateral to the levator palpebrae superioris, and later immediately below it.
3. The nerve fibres in the optic nerve have a spiral course.

The rotation was supposed by Vossius to occur after the 3rd month.

Strahl and Henckel postulated a rotation through 45° only and stated that it occurred before the 3rd month.

There appears to be good evidence (Deyl, Dedekind) that these conclusions are untenable and it seems likely that no rotation of the globe on its long axis occurs at all.

Considered from an evolutionary stand-point purely as an optical instrument and not in connection with the cortical powers of appreciation, the human eye leaves a certain amount to be desired. It is true that among the Mammalia it occupies a high place. It is (or should be) emmetropic and possesses a good range of accommodation, while most of the lower mammals are said to be hypermetropic. It also possesses a very highly specialised area of acute vision, the *fovea centralis*, which is only found developed to a like perfection in the larger anthropoids. It is, however, primitive and not far removed (save in the possession of a macula) from what one might call the basal type of vertebrate eye. It lacks certain specialised features which characterise some of the eyes of the lower mammals and the Sauropsida.

Two examples will make this point clear.

Firstly, the function of the human retina is to a certain extent impeded by the constant presence of circulating blood in the retinal vessels in front of the percipient layer, and also by the remnants of embryonic vessels in the vitreous. In the Sauropsida the hyaloid system in the embryo is reduced to a minimum so that the vitreous is very nearly acellular and homogeneous, while, instead of a network of vessels on the retina, the definitive intra-ocular blood supply is

Digitized by Illinois College of Optometry Library

represented by the pecten alone (which is in essence a mass of thin-walled capillaries projecting from the optic disc).

Secondly, the human eye, though it possesses the power of dark adaptation, lacks the extreme range of such adaptation found in the Carnivora. In these animals there is not only a very specialised iris, which allows of the alteration of the pupil from a state of complete circular dilatation to one of contraction into an extremely narrow vertical slit, but there is also present in the choroid a layer known as the *tapetum*, which, owing to its highly polished reflecting surface, probably helps to render appreciable much lower degrees of illumination than can be perceived by the human eye.

Therefore, both in birds and carnivores, we have an eye which is more nearly perfect as a percipient apparatus than the human eye, but which does not apparently lead to any corresponding increase in complexity of structure or function of the central nervous system. One cannot therefore look upon the human eye as having played any great part in the evolution of man, but one must consider it rather as a fairly simple organ rendered extremely valuable, not by great degrees of structural specialisation, but by the complexity of the cerebral centres with which it is connected.

Digitized by Illinois College of Optometry Library

Carl F. Shepard Memorial Library
Illinois College of Optometry
3241 S. Michigan Ave.
Chicago, Ill. 60616

646

III

THE LENS

The situation of the *lens plate* or *thickening* can be seen in embryos of 4 mm. It can be placed from the beginning, since it corresponds to that portion of the surface ectoderm which is primarily in direct contact with the neural ectoderm of the optic outgrowth. How this contact comes about has already been explained (see Fig. 7). In the 4 mm. stage, the neural groove has completely closed, and the optic outgrowths are present as definite primary optic vesicles in communication only with the cavity of the central nervous system through their wide stalks. Their outer faces are still in direct contact with the surface ectoderm. This contact is not a close adhesion, a distinct chink or gap always appearing between them after fixation. This gap is, however, usually crossed by fine strands of protoplasm uniting the two surfaces. At this stage both the neural ectoderm of the optic vesicle and the surface ectoderm are formed of a single layer of cells, cubical in shape and entirely undifferentiated.

Just after this stage those cells of the surface ectoderm which are in direct contact with the vesicle begin to assume a columnar form and appear to undergo fairly rapid division, with the result that the nuclei lose their arrangement in a single row, become uneven and tend to present the appearance of two or more rows of cells superimposed: but from a careful study of sections, both of this and the succeeding stages up to the separation of the vesicle, most observers[1] have come to the conclusion that only one layer of cells is present, the nuclei being often at opposite ends of the cell in contiguous cells.

The *lens plate* then can be seen in embryos of 4·5 mm.

As has already been mentioned, there is experimental evidence to shew that the lens plate represents a reaction on the part of the surface ectoderm to a stimulus supplied by the contact of the optic vesicle and is not in any other sense a purely local development.

Fig. 36 is a semi-diagrammatic section through the whole head at the level of the primary optic vesicles of a 4 mm. human embryo. The situation of the lens plate can be seen. In this embryo there were no mesoderm cells between the lental area and the optic vesicle, though mesoderm has been figured here at this stage by some observers. The stage at which mesoderm grows in here appears to

[1] E.g. Rabl, Bach and Seefelder.

Digitized by Illinois College of Optometry Library

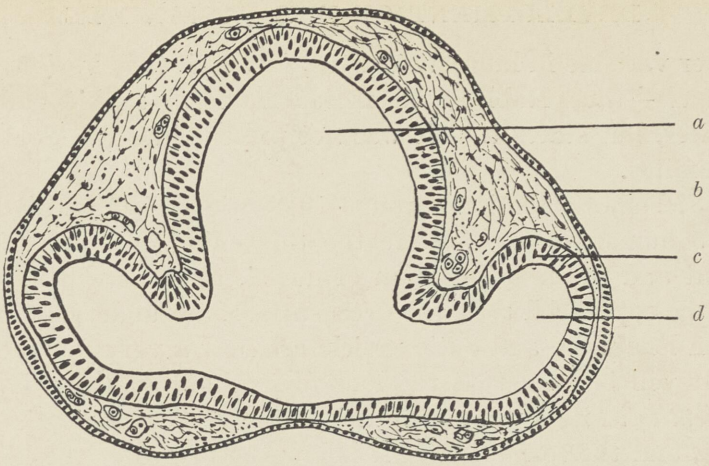


Fig. 36. Transverse section through anterior part of fore-brain and optic vesicles of a 4 mm. human embryo after Seefelder. *a*, cavity of fore-brain; *b*, surface ectoderm; *c*, wall of optic vesicle; *d*, cavity of optic vesicle.

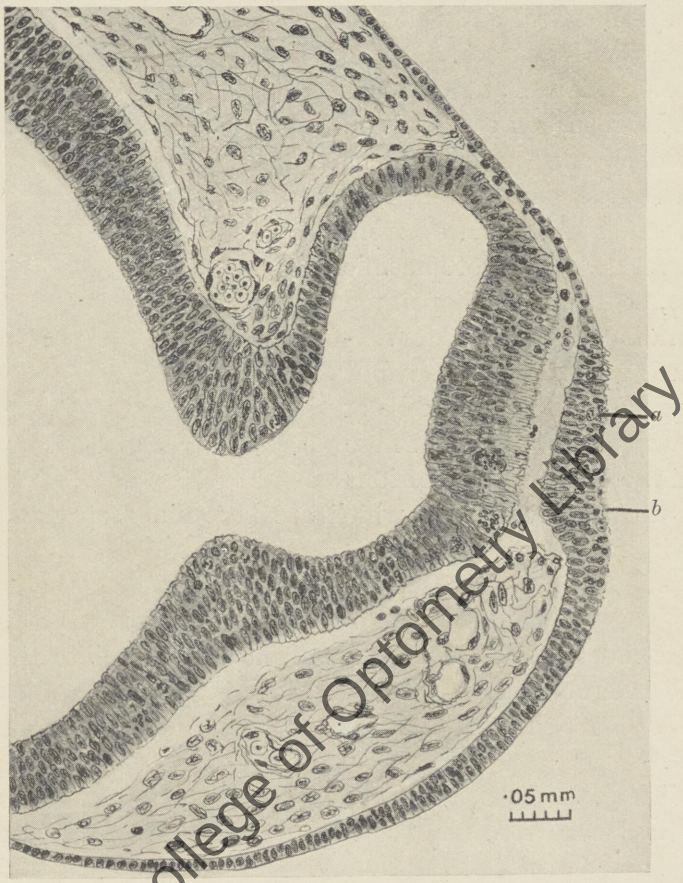


Fig. 37. Section through the lens plate and primary optic vesicle of a 4·5 mm. human embryo. *a*, cell in lens thickening undergoing mitosis; *b*, fovea lentis.

Digitized by Illinois College of Optometry Library

be rather variable in human embryos, just as it is in various species of animals—thus Rabl found mesoderm in a rabbit embryo of 13 somites, but states that it was not present in a duck or a lizard of 32 somites.

Fig. 37 shews a section through the optic vesicle and lens plate of a 4·5 human embryo. Here the thickening of the ectoderm is apparent and the multiplication of nuclei, three of which, situated nearer the superficial than the deep surface, are undergoing mitosis. Between lens plate and optic vesicle are now a very few mesoderm cells. It will be seen that the lens plate shews a slight depression (*fovea lentis*) in its lower part. This is the earliest indication of the lens pit, and the formation of it below the centre of the lens plate is characteristic of mammalian embryos and distinguishes them from other vertebrates, in which the lens plate is symmetrical and thickest and deepest in its centre. Fig. 38 shews the lens plate of an Acanthias embryo (Dogfish) for comparison.

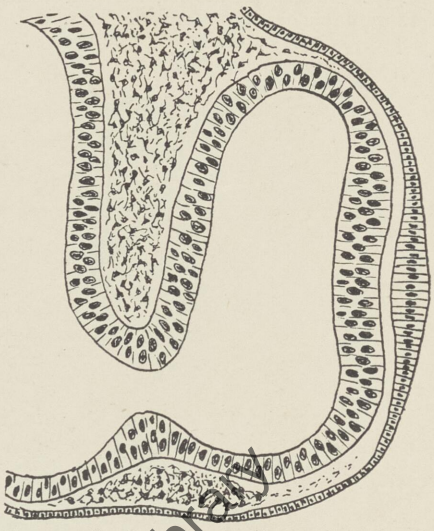


Fig. 38. Optic vesicle and lens thickening of a Dogfish (Acanthias) embryo.

If the deep surface of the lens plate in Fig. 37 be examined, it will be seen that projecting from it are several small protoplasmic processes, cone-shaped, pointed and extending across the intervening space towards similar but smaller processes from the cells of the primary optic vesicle. These represent the drawn-out adhesions between the two ectoderms which are becoming separated at this stage by ingrowing mesoderm.

If the superficial surface of the ectoderm, both of the lens plate and of the rest of the head, be examined, it will be seen to consist of a single layer of cells only, though on the lens plate the surface is slightly irregular and mitoses are occurring immediately under it. Up to this stage, therefore, there is no differentiation of the surface ectoderm.

Now, if Fig. 39 be examined, several important changes will be found to have occurred. The section shews the eye of a 5 mm. human embryo. Invagination of the optic vesicle has occurred to form the optic cup and the slight depression below the centre of the lens plate in Fig. 37 has deepened to form a definite lens pit. The lens pit

Digitized by Illinois College of Optometry Library

itself is not symmetrical, being deeper below than above. Its wall is still composed of a single layer of cells, but with the nuclei arranged at different levels. The cone-shaped protoplasmic projections from the deep surface are more marked than in the 4·5 mm. embryo and direct and obvious continuity is established through them with similar projections from the inner (retinal) layer of the optic cup. Between the lens and the optic cup there are still only a very few mesoderm cells, but these are increasing in number and becoming



Fig. 39. Section through the optic cup and lens pit of a human embryo of 5 mm.

definitely vaso-formative in character. Indeed, at the lower part of the cup, an endothelium-lined blood space containing nucleated foetal erythrocytes can be seen passing into the cup[1]. These strands of vascular mesoderm appear to interlace with the ectodermal strands connecting lens and retina, intersecting these at more or less right angles.

We must now turn our attention to the superficial aspect of the surface ectoderm. If this be examined over the whole body of the embryo, it will be found that here and there a single flattened cell

[1] Fig. 40 shews the complete series of sections through the lens pit of the eye seen in Fig. 39. The mesoderm can be seen entering below.

Digitized by Illinois College of Optometry Library

can be seen lying superficial to the cubical epithelial cells of the surface. These superficial cells do not even begin to form a layer at this stage, but they are the earliest representatives of the flattened (squamous) cells which, soon after this stage, will cover the whole body of the embryo. Thus the differentiation of the surface ectoderm begins by the formation of two layers: (1) a superficial or *epitrichial* layer of flat cells and (2) a deep or *nervous* layer of cubical cells. The formation of the superficial layer is at its inception most marked on the floor of the lens pit and in Fig. 39 a whole mass of these epitrichial

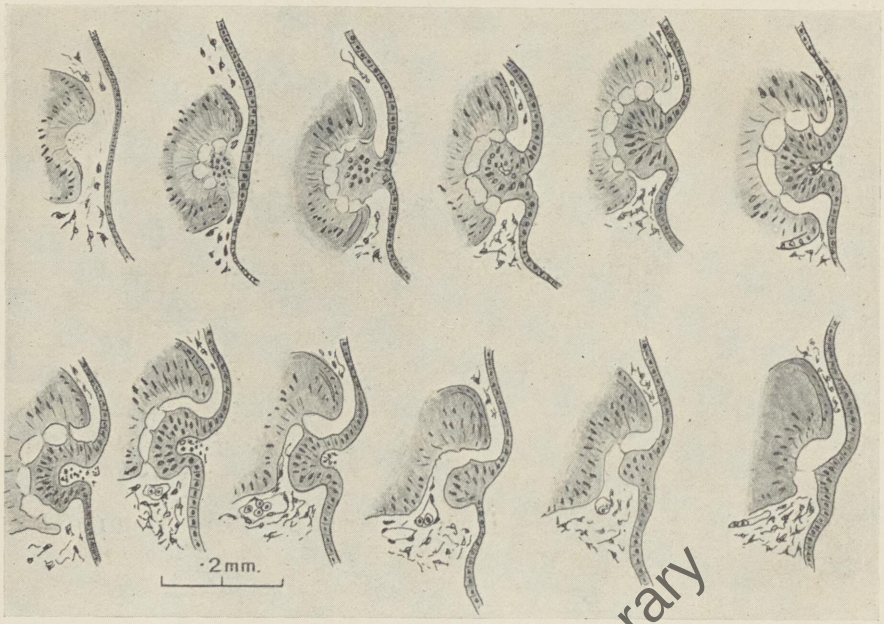


Fig. 40. Serial sections through the developing lens of the embryo in Fig. 39.

cells can be seen filling the lens pit, lying loosely on its surface and seemingly not very strongly adherent to it.

This differentiation of the surface ectoderm into two layers occurs in all vertebrate embryos, but the stage at which it appears relative to the degree of development of other ectodermal derivatives, notably the lens pit, seems to be very variable. It may be that the time of formation of the lens pit, considered in relation to the degree of specialisation of the skin and the auditory vesicle, may depend on the relative importance of the sense of sight in the animal's subsequent life. For example, in some of the primitive fishes (e.g. *Ceratodus Fosteri*—Australian mud-fish) the lens thickening does not appear till differentiation of the two layers of the ectoderm is complete,

Digitized by Illinois College of Optometry Library

while in birds it appears, and the pit forms, before such differentiation has even begun. This corresponds with the greater importance of the sense of sight in birds. Again, in rabbits, the auditory vesicle develops and separates from the surface before the lens pit appears, while in birds and lizards it does not. In man the lens pit and the commencing differentiation of the ectoderm appear together.

In those animals (e.g. most fish, other than Selachians, and some amphibians) in which the lens plate only appears after the formation of the two layers of the surface ectoderm, it is easy to see that the lens is formed entirely from the deep or nervous layer of the ectoderm, the superficial layer passing over it unchanged and not shewing any depression or pit. The lens is an invagination or thickening of the *deep layer only* and there is no lens pit. Any cavity which may be present in the separated lens vesicle in these animals is a secondary formation and is not a cavity made by invagination from the surface.

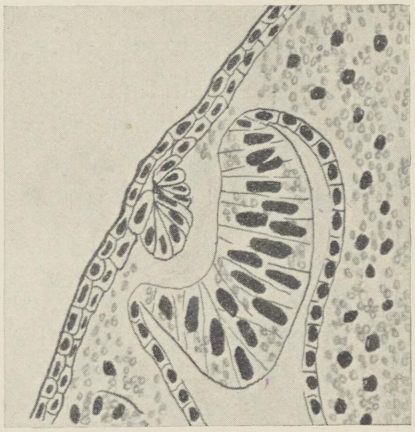


Fig. 41. The developing lens of *Ceratodus Fosteri* shewing involvement of the nervous layer of the surface ectoderm only.

Fig. 41 shews the developing lens of a *Ceratodus* embryo which has no lens pit, and in which the superficial layer of the ectoderm is not at all involved. In those animals (i.e. mammals) in which differentiation of the ectoderm occurs *pari passû* with invagination of the lens plate, the cells of the lens plate also undergo differentiation and an epitrichial layer is formed on the floor of the lens pit. As the lens pit closes, these cells get shut up inside it. This appears to be purely fortuitous and, as they have no real part to play in the development of the lens, they soon degenerate and disappear[1]. These cells can be seen very well developed and filling the lens pit in the embryo in Fig. 39. Their distinction from the cells of the wall of the lens pit is very marked.

Fig. 42 shews the next stage of development of the lens (*circa* 7 mm.). The lens pit has deepened and its opening has constricted so that it can now be described as a *vesicle* connected with the surface by a *stalk* through the centre of which still runs a narrow

[1] *Per contra*, in *Lacerta viridis* and other Sauropsidans in which the differentiation of the two layers of the surface ectoderm does not occur until after the closure of the lens vesicle, no free epitrichial cells are found in the cavity of the vesicle.

Digitized by Illinois College of Optometry Library

channel connecting the lumen of the vesicle with the exterior (see Figs. 27 and 42). Inside the lens vesicle are the fast disappearing cells of the epitrichial layer. They lie sometimes free in the cavity, sometimes adherent to its wall. In man they have all disintegrated by 16 mm.

In some amphibia they occasionally seem to fall into line with the cells of the wall of the lens vesicle and to take part in its formation.

The lens stalk becomes more constricted, its lumen disappears and the lens vesicle separates from the surface ectoderm at the 9 mm. stage.

Fig. 43 is drawn from an embryo of 10 mm. in length. The lens is now a hollow sphere, its wall composed of a single layer of short columnar cells, the nuclei of which, being at different levels in adjacent cells, lead to the appearance of a double layer in places. At this stage, the thickness of the wall of the vesicle is approximately 0·04 mm.; it is roughly spherical in shape, but its antero-posterior diameter is slightly greater than its side to side measurement. Its radius of curvature averages 0·1 mm.

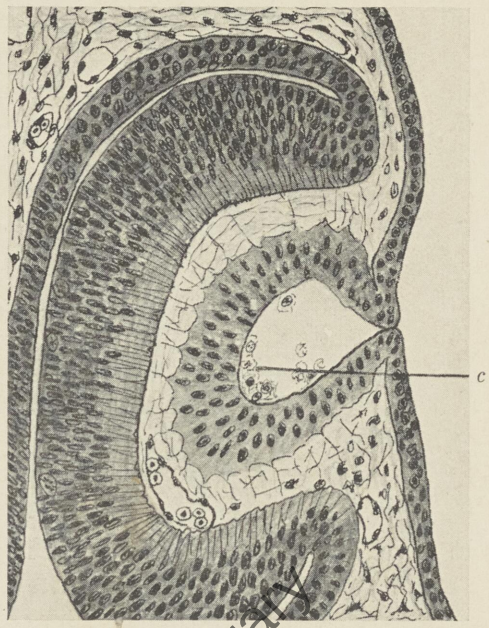


Fig. 42. Section through the lens vesicle of a human embryo of 7 mm. (after Bach and Seefelder). *c*, cells in cavity of lens vesicle.

As soon as the vesicle separates from the surface, mesoderm grows in between the two and all trace of the point of attachment of the vesicle to the surface ectoderm is immediately lost. Mesoderm has also increased in the interior of the optic cup and this now contains many large blood vessels. In spite of this, however, careful examination will still reveal traces of the old direct protoplasmic continuity between lens and retina. (This is most marked in Fig. 43 in the region of the upper part of the optic cup.)

In all vertebrates the lens appears to go through this stage of a hollow vesicle. In most of them the lumen of the vesicle is circular on section and is the direct outcome of the invagination, as it is in man; but in Selachians the cavity is of secondary formation, only appearing after separation of a solid mass of cells from the surface.

Digitized by Illinois College of Optometry Library

After separation of the lens vesicle from the surface ectoderm, it begins to differentiate and undergoes a series of important changes. It must be clearly realised at the outset that *only the cells of the deep or inner half of the wall of the lens vesicle undergo any marked differentiation*. The cells of the anterior half are arranged (by the 11–12 mm. stage) in a single row of cubical cells, their nuclei now all on the same level. As the lens grows, the number of these cells increases *pari passû* with it, and they form the anterior epithelial capsule,

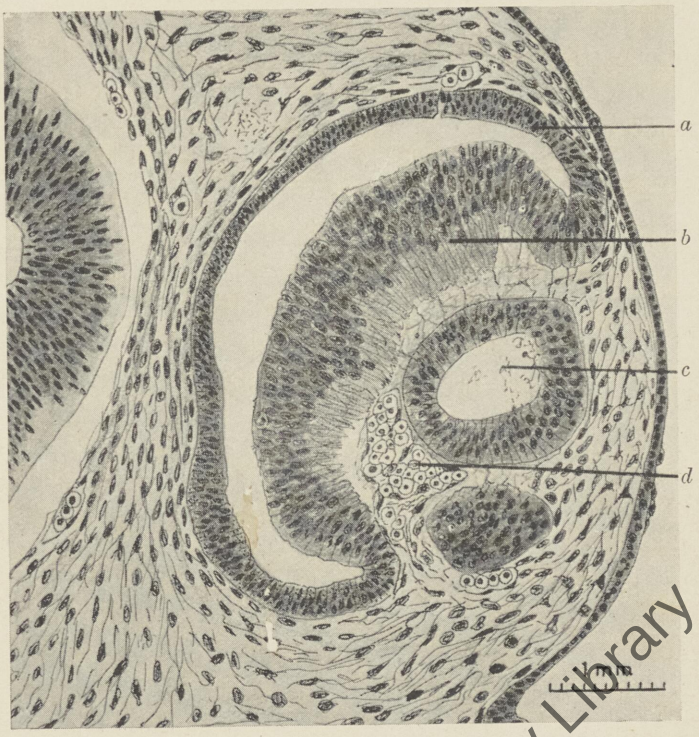


Fig. 43. Section through the eye of a human embryo of 10 mm. *a*, outer layer of optic cup; *b*, inner layer of optic cup; *c*, lens vesicle; *d*, blood vessel.

but they retain throughout life their original characteristics of a simple cubical epithelium. They become slightly flatter as time goes on, but they do not alter in character at all.

On the other hand, *the cells of the posterior wall form the first of the lens fibres to appear*, and it must be clearly understood that *the whole of the adult lens* (except the anterior epithelium) *is formed from the cells of the posterior wall and the equatorial region*, the anterior wall of the lens vesicle taking no part in the formation of lens fibres. From the 10 mm. stage the posterior cells increase in length so that they soon form a columnar epithelium, and the lumen of the vesicle

Digitized by Illinois College of Optometry Library

becomes almost crescentic instead of circular (see Fig. 44) in consequence. As these cells grow they encroach on the lumen still more, so that by the 13 mm. stage it has become completely crescentic on section.

Fig. 44 is a section through the lens of a 12 mm. embryo, shewing an early stage of this elongation of the cells of the posterior wall, and Fig. 45 is a section through the lens of a 13 mm. embryo in which growth is slightly more advanced.

Although the cells of the posterior wall grow at the expense of the cavity of the lens vesicle, their nuclei appear to migrate slowly during growth so that they are always nearer the anterior than the posterior end of the cell. These cells of the posterior wall can now be spoken of as primitive lens fibres. They are homogeneous and clear, and each one has a single darkly staining nucleus. They are longest and straightest at the posterior pole, and decrease regularly in length and increase in curvature (being concave towards the sides of the lens) as they approach the equatorial region, where they merge into the cubical cells of the anterior wall of the vesicle. The antero-posterior diameter (0·24 mm.) of the vesicle is still slightly greater at the 12 mm. stage than that from side to side (0·2 mm.). The thickness of the posterior wall is 0·11 mm. and of the anterior wall still 0·04 mm.

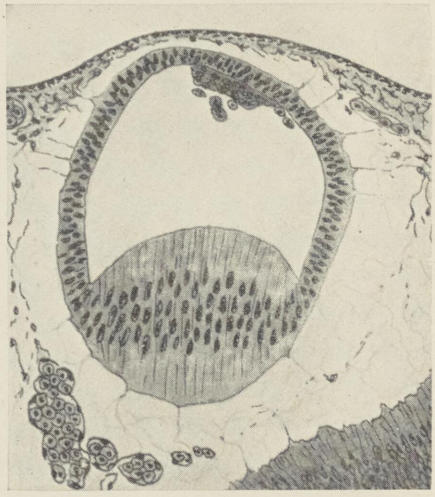


Fig. 44. Section through the lens vesicle of a human embryo of 12 mm. Note the elongation of the cells of the posterior wall, the so-called "epithelial cells" included in the lens cavity, and the remains of the protoplasmic adhesions stretching between the lens and surrounding structures. The surface ectoderm is seen in the upper part of the drawing and a small piece of the retinal wall on the right below.

The lumen of the vesicle is crescentic and contains the fast disintegrating remnants of the free cells seen in the previous diagrams.

One other feature must be noted. The apparent cone-shaped projections from the vitreous surface of the lens, which were noted in previous stages, have entirely disappeared by the 13 mm. stage. The outline of the lens is very clear cut and a hyaline capsule is now present. This can be seen as a thin highly refractile line at the posterior pole of the lens, where it has separated from the lens fibres during fixation. The small space between it and the lens is filled

Digitized by Illinois College of Optometry Library

with a finely granular albuminous coagulum. The hyaline capsule is probably secreted by the cells of the lens vesicle, more especially those of the anterior wall, since it is always rather thicker in front than behind. It is never cellular. Outside the hyaline capsule in Fig. 45 can be seen the mesoderm of the fibro-vascular capsule which is by this stage well formed.

In the 16 mm. stage, the cavity of the lens vesicle has become obliterated by the lengthening of the cells of the posterior wall. It is, of course, potentially present as a chink between the anterior ends of the primitive lens fibres and the cells of the anterior epithelium,

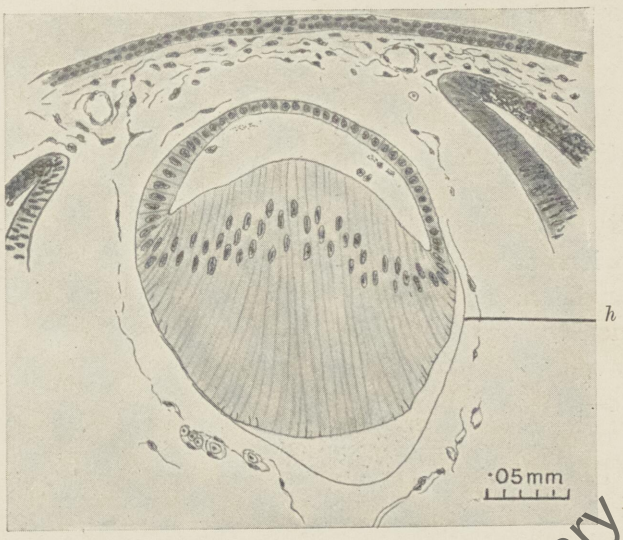


Fig. 45. The lens of a 13 mm. human embryo. Note the further elongation of the cells of the posterior wall, the decrease in number of the included cells and the appearance of a hyaline capsule (*h*).

but it does not shew as a definite space, except occasionally when the anterior epithelium has become detached during preparation. There are never any cell remnants in it at this stage.

The antero-posterior measurement is still greater than that from side to side (i.e. 0·35 mm. : 0·30 mm.) as the cells in the equatorial region have not yet started to divide and form lens fibres.

Each fibre can be seen to consist of a single cell with nucleus. They pass from back to front of the lens. Those nearest the sides are short and shew a curve concave towards the equator; those further in are straighter or curved towards the centre of the lens; those in the centre are straight. This arrangement persists unchanged up to 26–30 mm. except that the lens gets larger as a whole

Digitized by Illinois College of Optometry Library

and the nuclei of the most central fibres begin to disappear, swelling up and refusing to take the stain. At the same time the nuclei at the equator increase in number and become crowded together in readiness for further divisions, since it is from this region that all the new lens fibres will be formed. The central fibres are now completed, will not grow any more and will not divide.

These primitive lens fibres remain at the exact centre of the lens throughout life and can be recognised as the dark (optically empty) region between the two plano-convex inner embryonic nuclei, seen when the living lens is examined with the narrow beam of the slit-lamp.

If the lens is viewed in equatorial section (i.e. cut in planes parallel to a plane passing through the equator all round) its fibres will, of course, be seen cut transversely instead of longitudinally, and an entirely different picture will result. The usual longitudinal section rather gives one the impression of a structure resembling an onion, an impression strengthened by those pictures —much favoured by the older anatomists—of the hardened lens split open and peeling off in layers. This idea must be modified by keeping always in mind the picture of the equatorial section too, which, as Rabl has pointed out, makes the lens look much more like an orange than an onion. An equatorial section of an adult lens has rather the appearance seen in Fig. 46 (from Rabl) which shews a sector of the lens of *Lacerta agilis* in equatorial section.

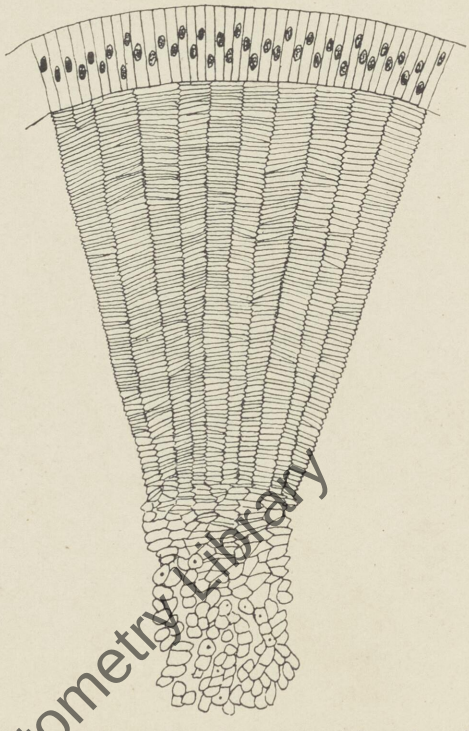


Fig. 46. A portion of an equatorial section of the lens of an adult *Lacerta agilis* (after Rabl).

An equatorial section of a human foetal lens (Fig. 47) shews much the same arrangement.

Fig. 48 shews a longitudinal section of a lens of an embryo of 26 mm. Note the aggregation of nuclei in the equatorial region. Immediately after the 26 mm. stage the secondary lens fibres begin to form outside the primary ones (which came from the cells of the posterior wall of the vesicle). The secondary fibres, from now on,

Digitized by Illinois College of Optometry Library

grow throughout the whole of intra-uterine and post-natal life, though, of course, at a rapidly decreasing rate. They come from the cells in the equatorial region where the cubical epithelium of the anterior capsule passes into the long lens fibres.

As each new lens fibre formed here grows, its *anterior end* passes forwards, in front of the anterior ends of the lens fibres behind it and deep to the cubical epithelium of the anterior surface, towards the anterior pole, while its *posterior end* passes backwards deep to the hyaline capsule towards the posterior pole.

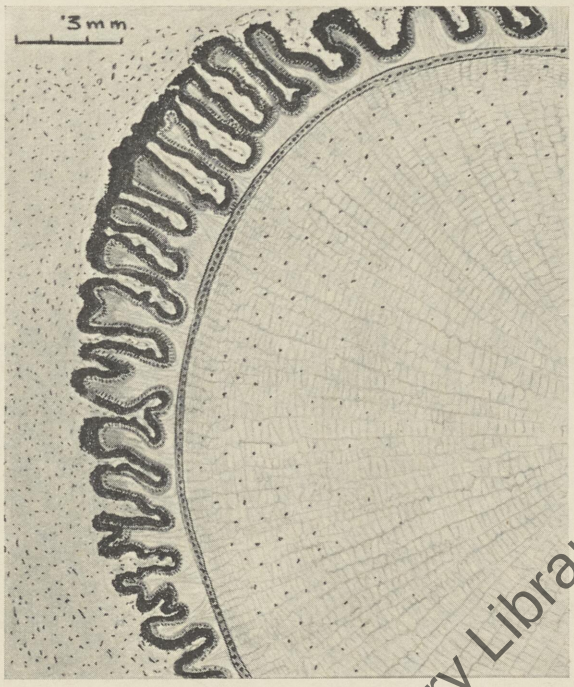


Fig. 47. Equatorial section through human foetal lens (7·10 mm.). The ciliary processes and the bundles of fibres of the suspensory ligament are also seen.

In this way the new lens fibres form a layer encircling and covering the surface of the primitive lens fibres, which thus get somewhat compressed and come to lie in the centre of the lens (Fig. 49). New lens fibres are, of course, being formed simultaneously all round the equator of the lens. Each of these fibres is exactly the same length as every other fibre formed at the same time, and just a little longer than each of the fibres formed a few hours or days before. But not one of the fibres formed at any time is quite long enough to reach from the exact centre of the lens in front to the exact centre behind.

Digitized by Illinois College of Optometry Library

If they were, they would all converge on a point behind and another in front of the lens, but as they are not of such a length, the region of meeting is linear and the pattern formed by these lines of meeting of the fibres is known as the *suturing* of the lens. The simplest suture possible is a straight line and this is found in most of the lower vertebrates and even among the mammals.

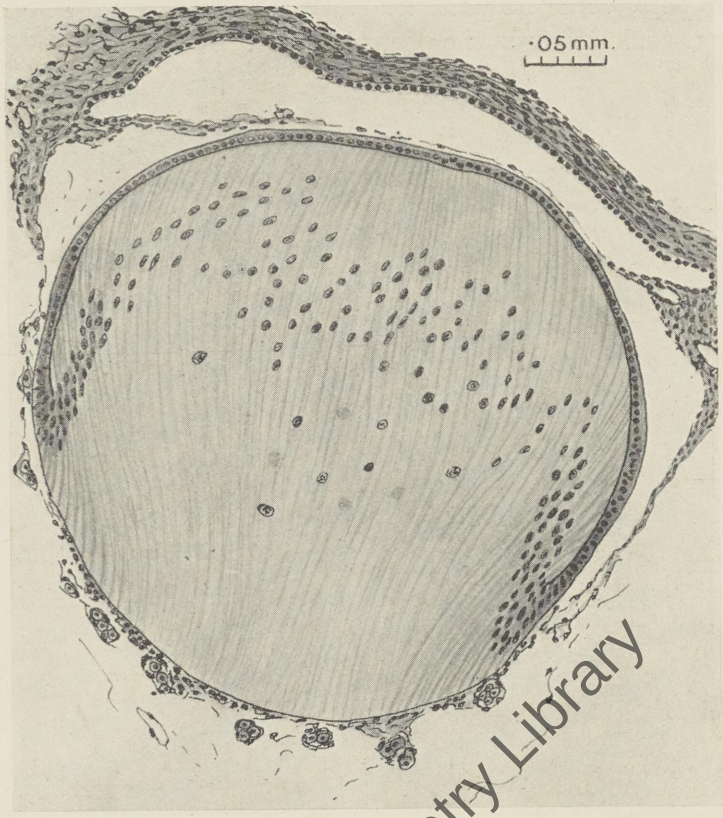


Fig. 48. Transverse section through the lens of a 26 mm. human embryo. The cornea and the anterior chamber are seen in the upper part of the figure. Branches of the hyaloid artery are in contact with the lens capsule posteriorly (below in the figure).

Fig. 50 shews how the sutures arise. *A* shews an imaginary lens without sutures in which all the fibres run to and from the centre back and front, *B* shews a lens with a linear horizontal suture on one side and a linear vertical one on the other (e.g. Selachian). It will be seen that all the fibres shewn are the same length and that those which reach nearest the centre in front, fall farthest short of the centre behind and *vice versa*. The suture itself is in reality a potential cleft between the ends of fibres abutting on each other.

Digitized by Illinois College of Optometry Library

These ends are usually swollen and flattened. (See the posterior suture in Fig. 52.)

In the human embryo the sutures at their first appearance are linear, the anterior one horizontal, the posterior one vertical (like the adult Selachian lens, Fig. 50 *B*), but this stage is very transient and the straight lines soon branch, so that a tri-radiate form resembling the letter Y is produced. That on the anterior surface of the lens is an erect Y, while that on the posterior is inverted ⅄. *C* in Fig. 50 shews the arrangement of the fibres and how the sutures are produced. It is obvious that the pattern on one side of the lens must be the reverse of that on the other, and that, in any section in which the fibres approaching one suture are cut longitudinally, those approaching the opposite one must be cut transversely. This lapping of the secondary lens fibres over the primary ones and the consequent formation of

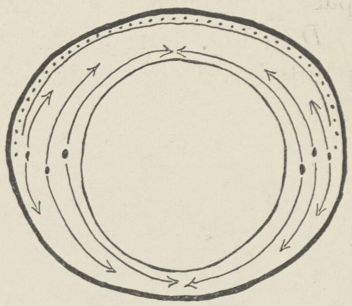


Fig. 49. Scheme to shew the direction of extension of the cells of the equatorial region as they grow to form lens fibres. The central circle represents the portion of the lens formed from the cells of the original posterior wall of the lens vesicle.

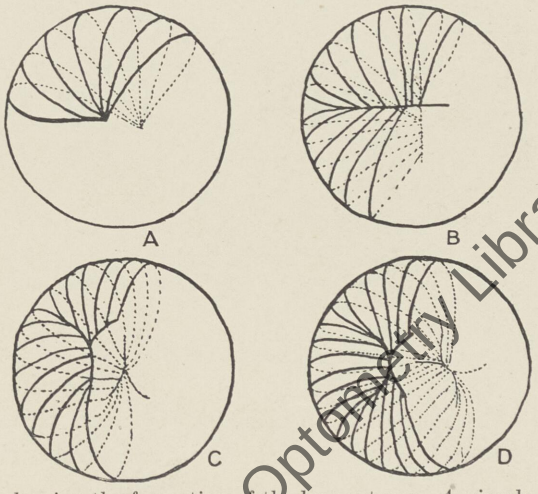


Fig. 50. Diagram shewing the formation of the lens sutures. *A*, simple arrangement with no sutures. *B*, linear sutures only (found in adult dogfish). *C*, the Y sutures of the human embryonic nucleus. *D*, four-pointed star of human adult nucleus.

sutures is apparently an arrangement to maintain the shape of the lens. If new fibres were constantly being formed at the equator but did not overlap the older ones, the lens would increase rapidly in circumference, but not in depth, and would resemble a flat disc. The meeting of the fibres in lines allows of much

Digitized by Illinois College of Optometry Library

greater precision of joining than would be possible if they all converged on a point—in the latter case a pit would probably be formed which would interfere with the regular refraction of light passing through.

D in Fig. 50 represents the condition when the suture is a four-pointed star (e.g. adult nucleus—see later).

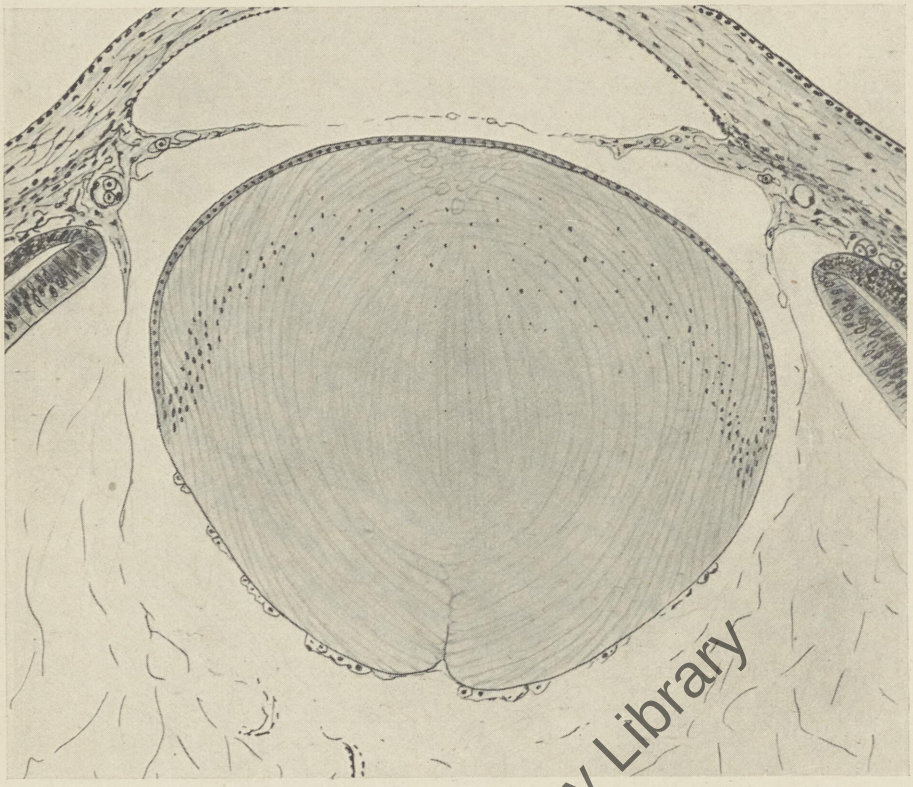


Fig. 51. Section of the lens of a 35 mm. human embryo, shewing the beginning of the lens sutures.

Fig. 51 shews the lens of a 35 mm. embryo. With the addition of secondary lens fibres formed from cells in the equatorial region, the shape of the lens as a whole has been modified, so that the diameter from side to side (i.e. 0·7 mm.) is now greater than the antero-posterior diameter (i.e. 0·6 mm.). This change of shape becomes apparent soon after the 20 mm. stage, at which stage the lens is almost completely spherical. It will be seen (Fig. 51) that the sutures are well formed and already fairly deep. The posterior suture appears as a definite linear chink or crack at the posterior pole, while the situation of the anterior one is only shewn by the aggregation of a number of fibres

Digitized by Illinois College of Optometry Library

cut transversely at the anterior pole. The reason of this appearance has been explained already.

Sections shewing the posterior suture extending from the surface to the central (earliest formed) lens fibres, serve to impress on us the fact, easily overlooked, that the sutures are not only linear markings on the surface of the lens, but also have a depth extending through the lens in an antero-posterior plane.

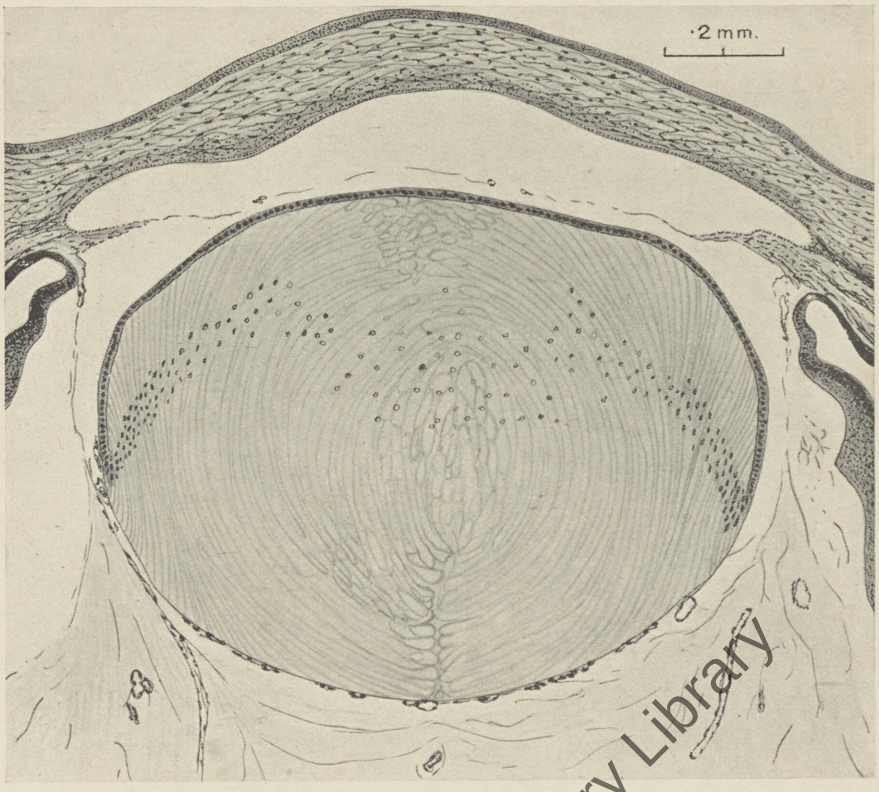


Fig. 52. Section through the lens of a 48 mm. human embryo.

Fig. 52 is a section through the lens of a 48 mm. embryo and resembles on the whole Fig. 53 which shews the lens of a 65 mm. human embryo.

The following points should be noted:

The cubical epithelium of the anterior capsule, which has not changed in appearance since the 13 mm. stage.

The cells of this epithelium passing at the equatorial region gradually into the lens fibres proper.

The alteration in curve of the lens fibres as they approach the centre, short ones at the equator being concave outwards, the next

Digitized by Illinois College of Optometry Library

showing a double curve, concave outwards in their centre and convex outwards at either end, and the ones that take part in the formation of the sutures being convex outwards throughout their whole extent.

The shape of the lens. This resembles still more the adult form, the antero-posterior diameter being now 1·38 mm. and that from side to side 1·75 mm.

The condition of the nuclei. Those in the equatorial region are deeply stained and closely packed, those in the centre are faintly

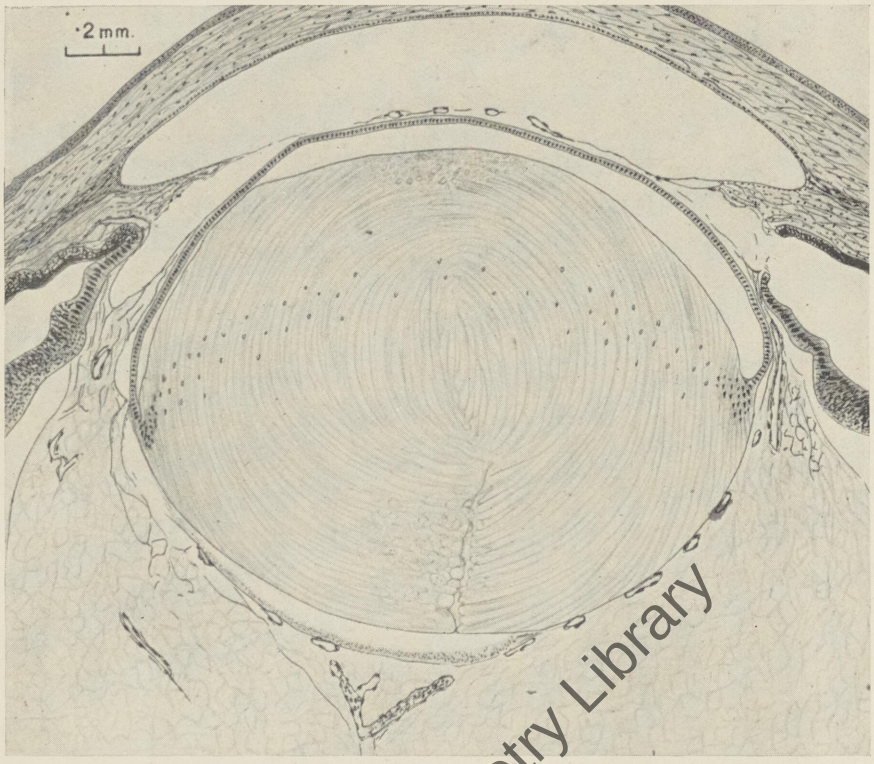


Fig. 53. Section through the lens of a 65 mm. human embryo.

stained and in process of disintegration. Very few nuclei can be recognised after this stage in the central (primitive) lens fibres.

Fig. 54 is a high-power view of a portion of the equatorial region of the lens seen in Fig. 53.

From now onwards growth of the lens takes place by the addition of new fibres from cells in the equatorial region with consequent compression of the central fibres. As the lens increases in size the sutures become more complex. The Y sutures may occasionally shew branchings at the extremities of their limbs, but more often

Digitized by Illinois College of Optometry Library

the Y arrangement becomes merged into a star shape (sometimes having as many as nine points or rays) which may be found on the surface of the lens at or soon after birth (see Fig. 55).

This alteration in the pattern of the sutures continues throughout life. At birth each Y lies almost beneath the capsule. During child-

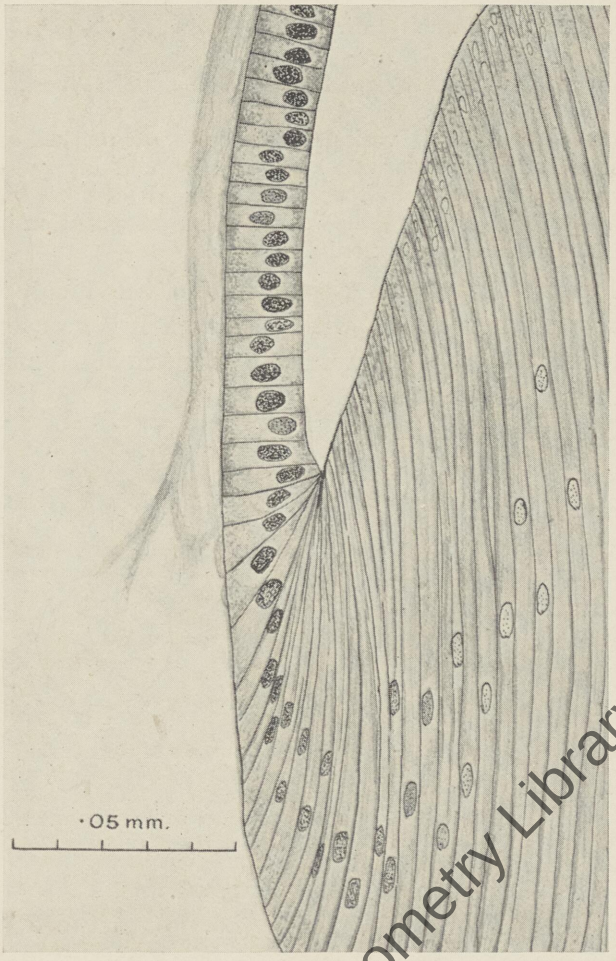


Fig. 54. High-power view of a portion of the equatorial region of the lens shewn in Fig. 53.

hood they appear to lie more deeply in the lens, the superficial suture now having the form of a star. In adult life the Y and the star are overlayed by a further stratum of fibres, the suturing of which is variable but most often consists of a vertical line which bifurcates above and below Y. In old age yet a further layer has been added, the suturing of this being in the form of a branching star. Fig. 55 shews these patterns diagrammatically.

Digitized by Illinois College of Optometry Library

These various layers of the lens which shew different suture patterns on their surfaces possess slightly different indices of refraction, so that, if the living lens is examined in a very narrow beam of light, one can make out faint lines of demarcation between them. In this way four zones have been recognised, as follows:

(1) A *central dark space* representing the portion of the lens which has no sutures, namely, the primitive lens fibres developed from the cells of the posterior wall of the lens vesicle.

(2) A *foetal nucleus* formed during intra-uterine life. This may be divided into an inner and outer portion.

(3) An *adult or adolescent nucleus* formed during adolescence and early adult life.

(4) A *cortex* covering these various strata and most marked in old age.

This classification[1] of the lens zones has been worked out by Vogt and other investigators with the slit-lamp, and certainly appears to be much more consonant with observed facts than was the older classification into two zones or layers, a nucleus and a cortex only.

The first-formed lens fibres appear to be the most transparent, which property they share with other early embryonic tissues. The later fibres become progressively less and less transparent, so that in extreme old age the presence of definite opacities in the equatorial region of the cortex is so common as to be almost the rule.

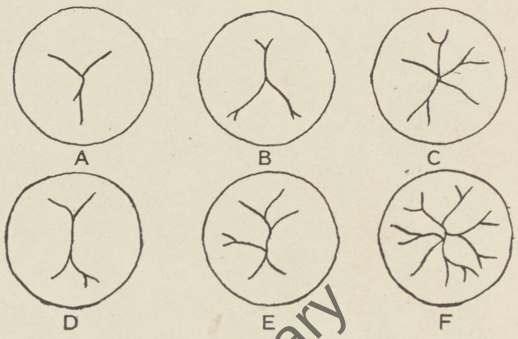


Fig. 55. The sutures of the human lens. *A*, anterior suture of inner foetal nucleus. *B*, posterior suture of inner foetal nucleus. *C*, suture of outer foetal nucleus. *D*, of adult or adolescent nucleus. *E*, another pattern of this. *F*, of cortex.

The alteration in shape of the lens during development appears to be due to two factors:

(*a*) The growth in length of the cells of the posterior wall of the vesicle, and

(*b*) The addition of secondary lens fibres in the equatorial region.

At the beginning of development (i.e. up to the 25 mm. stage) the increase in size of the lens is practically entirely due to the first of these factors, so that the antero-posterior diameter of the lens is almost the same as the length of the cells of the posterior wall.

[1] This conception of the structure of the lens is a recent one and unfortunately there is still a certain amount of confusion with regard to the nomenclature of the various zones. This is due in part to the difficulty of translating and in part to the initial lack of knowledge of the times of appearance of the various layers. Thus, in translations from the German, the foetal nucleus is often called the embryonic, though it is now known to develop mostly after the 3rd month (at which time the developing individualbecomes, strictly speaking, a foetus). Similarly, the portion developing during adolescence is sometimes called the senile nucleus. Actually, in point of time, the central dark interval is *embryonic*, the zone of the Y sutures *foetal*, the next layer *adolescent* and the cortex *adult* and *senile*.

Digitized by Illinois College of Optometry Library

After the appearance of the secondary lens fibres, the antero-posterior diameter becomes considerably greater than the length of the cells of the posterior wall (i.e. the lens fibres of the *central* nucleus). This can be expressed graphically by plotting the value of the ratio

$$\frac{\text{antero-posterior measurement of lens}}{\text{length of cells of posterior wall of vesicle}}$$

against the stage of development of the embryo. It will be seen that the curve falls steeply during the time that the cells of the posterior wall do not completely fill the lens vesicle and then remains stationary to the 25 mm. stage, rising slowly as the secondary lens fibres appear.

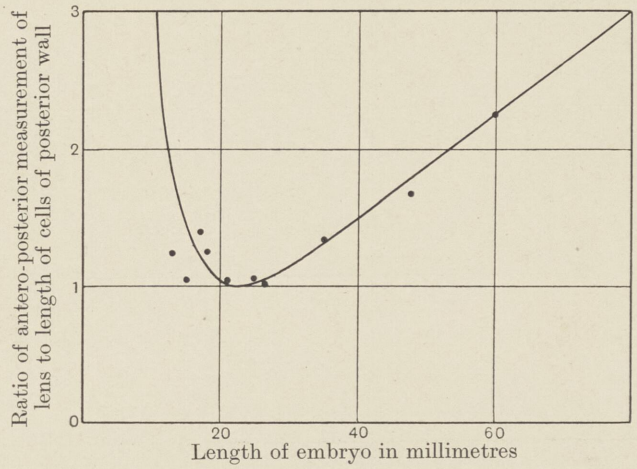


Fig. 56. Graph shewing factors in alteration of shape of lens.

The effect of the addition of the secondary lens fibres in the equatorial region on the shape of the lens can be shewn by plotting the ratio $\frac{\text{antero-posterior diameter}}{\text{equatorial diameter}}$ against the stage of development of the embryo. It will be seen that at the beginning, when the antero-posterior diameter is greater than the equatorial, the ratio is greater than one and that, as the lens becomes more spherical, the line of the graph falls, dropping steadily after 25 mm. as the secondary lens fibres come into being.

Congenital Abnormalities

The study of the development of the lens would naturally appear to be of value in the elucidation of congenital abnormalities of this organ, but, as a matter of fact, it does not throw much light on the subject. This is because, in the case of the lens, the commonest

Digitized by Illinois College of Optometry Library

abnormality met with is some form of opacity, and, as has just been pointed out, the quality of opacity is not found in any normal stage of development. Congenital opacities, then, must be looked on as pure aberrations, not arrests of development, and so far no certain cause can be found for them. The most that can be said with regard to their production is that it is possible from their situation to place fairly accurately the time at which the lens fibres concerned were formed, but whether the opacity arose at the same time or occurred as a subsequent degeneration, it is impossible to say.

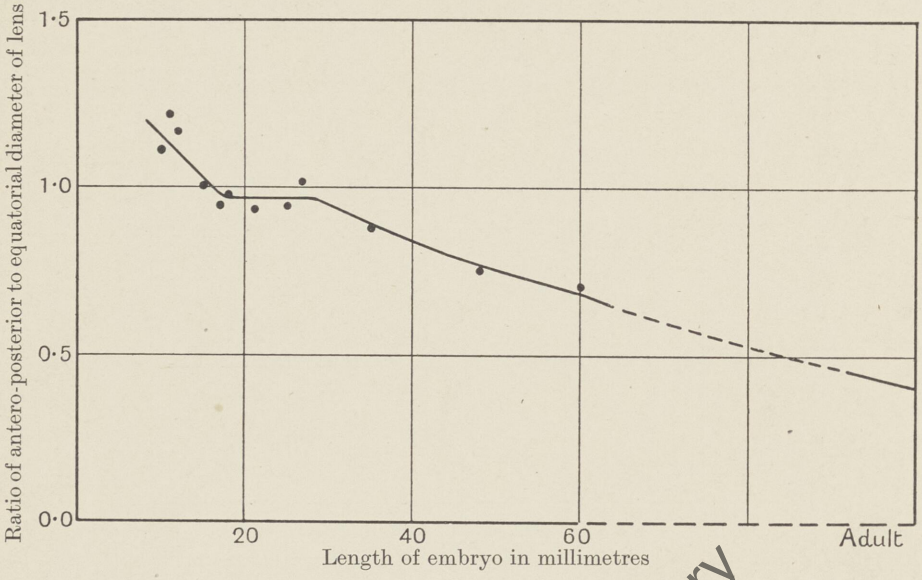


Fig. 57. Graph shewing effect on shape of lens of addition of secondary lens fibres.

There are, however, one or two rare defects of development of the lens alone which deserve mention:

(1) Delay of closure and separation of the lens vesicle from the surface ectoderm. If this occurs and lens fibres begin to form from the posterior wall, they may grow forward and protrude through the opening in the capsule. If this subsequently closes, an opacity of the anterior capsule will result. That delay of separation of the vesicle is possible has been shewn by Hess, who discovered the condition in a fowl embryo.

Delayed separation of the lens vesicle from the surface ectoderm must not be confused with another developmental defect usually called "delayed separation of the lens from the cornea." In this latter the lens is perfectly well formed and separated from the ectoderm, but, owing to delay or defect in the formation of the anterior chamber, the lens remains in contact with the mesoderm between it and the surface for too long, so that the growth of the

Digitized by Illinois College of Optometry Library

iris is interfered with. The condition has been described by Collins in a fowl embryo. The difference in time of the two aberrations makes it important to distinguish between them, the first occurring probably during the 4th week, the second during the 8th week, of intra-uterine life.

(2) Failure of development of lens fibres from the cells of the back wall of the lens vesicle. This leads to absence of the central portion of the lens. The cells in the equatorial region form lens fibres which are irregularly arranged, having no central mass round which to group themselves. The result is a congenital disc-shaped cataract.

The converse of this (congenital Morgagnian cataract) in which there is absence of the lateral lens fibres with an intact central nucleus, appears to be more in the nature of a secondary degeneration than a primary failure, since the capsule is distended with a milky fluid.

(3) Reduplication cataract. This is an interesting form of anterior opacity of the lens. There has been an intra-uterine (or more rarely post-natal) injury or defect of the anterior capsule together with a few of the lens fibres in direct contact with it. Healing has taken place with subsequent development of new (normal) lens fibres between the capsule and the originally defective fibres, so that the end result is a localised opacity of the anterior capsule, with a similar opacity deep to the first but separated from it by a varying depth of normal lens. It is possible to place the time of the original aberration by the depth of the reduplication from the surface.

Finally one must lay stress on two rather obvious points in connection with developmental defects of the lens.

Firstly, defects situated outside the "foetal nucleus" cannot be congenital, and *secondly*, defects may arise in post-natal life and yet be developmental, since the lens continues to develop throughout life[1].

[1] For abnormalities connected with the tunica vasculosa lentis and with the suspensory ligament see pp. 234 and 188.

Digitized by Illinois College of Optometry Library

IV

THE NEURAL ECTODERM

The neural ectoderm of the walls of the optic cup gives rise to the three regions of the uveal tract which can be recognised in the adult as:

A. *Pars optica retinae* or retina proper.

B. *Pars ciliaris retinae* or ciliary epithelium (subdivided into *pars plana* and *pars plicata*).

C. *Pars iridica retinae* or iris epithelium together with the *constrictor* and *dilatator pupillae* muscles.

The neural ectoderm of the optic stalk gives rise to

D. The optic nerve.

The *pars optica* will be dealt with first.

A. Pars Optica Retinae

The story of the development of the retina proper is that of the differentiation of the neuro-epithelium forming the wall of the invaginating optic *vesicle* at the 5 mm. stage. From the outer of the two walls of the optic *cup* is formed only the pigmented epithelial outermost layer of the retina, while the inner wall thickens considerably, undergoes a complex process of specialisation, and forms the remainder of the definitive retina from the outer limbs of the rods and cones to the internal limiting membrane inclusive.

Fig. 58 represents a section through the primary optic vesicle of a 4·5 mm. human embryo.

The stalk is widely open and is inserted at the lower part of the vesicle. This latter is in contact with the ectoderm which is beginning to form a lens thickening. It will be seen that even at this early stage a distinct difference is apparent between the somewhat flattened superficial wall of the vesicle (the part in contact with the lens plate) and the rest of it. This superficial or *outer* wall, which after invagination will become the *inner* layer of the optic cup, is thicker and already shews a separation into two zones, a deeper containing the nuclei and a superficial or marginal zone more or less free from nuclei.

Fig. 59 is a high-power drawing of a portion of the wall of the optic vesicle. The section goes through the upper part of the vesicle so that at the top of the drawing the thickened portion (outer wall of vesicle) is seen narrowing into the thinner. The thickened portion of the wall where differentiation is actively taking place measures

Digitized by Illinois College of Optometry Library

0·09 mm. in depth, while the thinner is 0·035 mm. only. The nuclei are arranged in 8–9 rows. They vary slightly in size, are oval and have a very darkly staining nucleolus and prominent chromatin net. Those nearest the cavity of the optic vesicle shew very frequent mitotic figures.

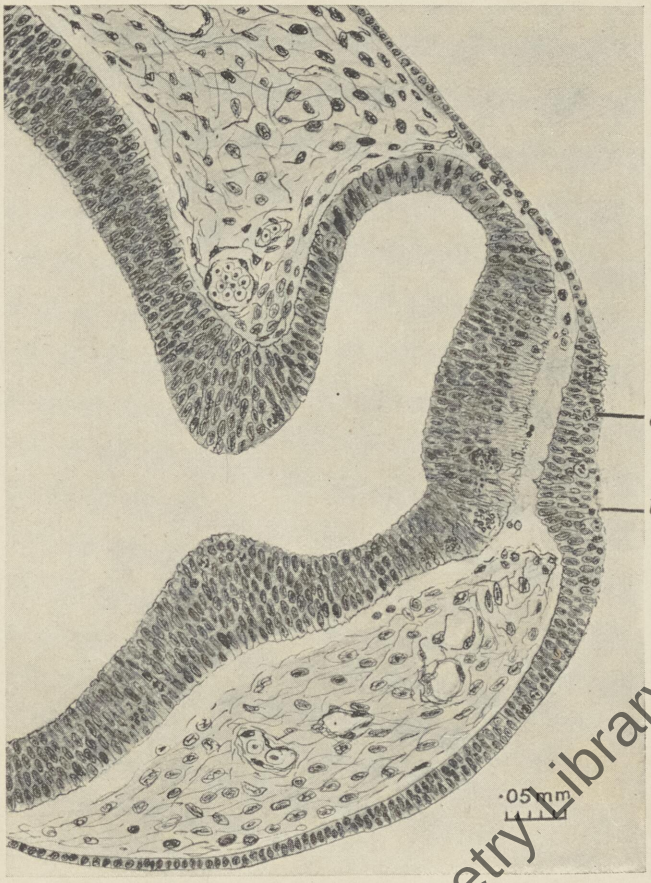


Fig. 58. Section through the lens plate and primary optic vesicle of a 4·5 mm. human embryo. *a*, cell in lens thickening undergoing mitosis; *b*, fovea lentis.

Fig. 60 shews five stages of karyokinesis taken from this layer. The dividing cells usually shew a cell outline but it is rather difficult to make out a boundary for the resting cells and the epithelium appears in parts like a syncytium. Karyokinesis is rare anywhere except in the layer nearest the cavity of the vesicle, but with care dividing cells can be found at other depths as well. In Fig. 59 one is seen (at *c*) just under the superficial surface in the lower part of the drawing. The superficial and deep surfaces of the epithelial wall

Digitized by Illinois College of Optometry Library

of the vesicle (seen in Fig. 59) should now be examined. The deep surface (that turned towards the cavity of vesicle) resembles the inner surface of the fore-brain and the rest of the central nervous system. It is sharply limited and from the surface project short fine cilia (i.e. it is formed by a ciliated epithelium exactly resembling that

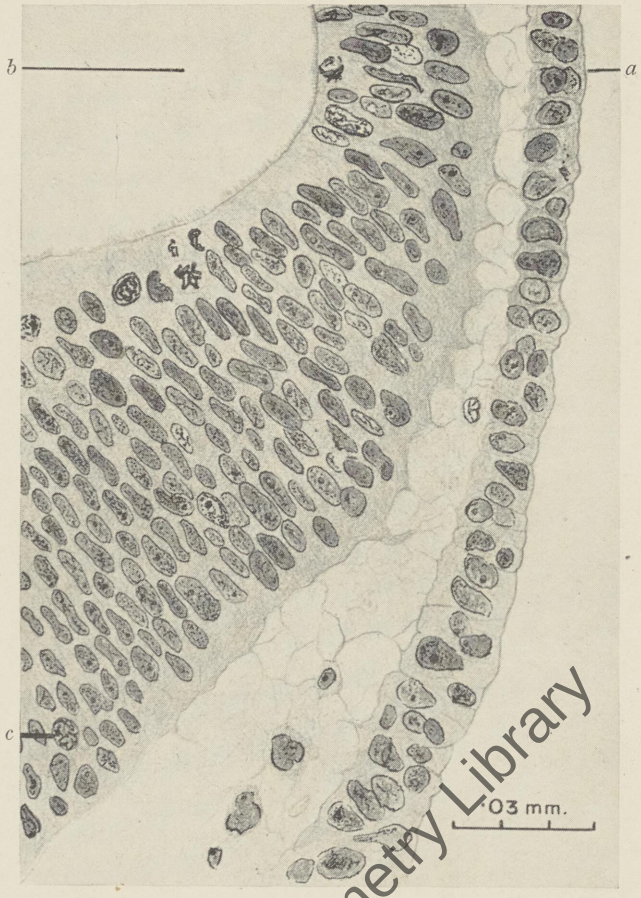


Fig. 59. Section through the upper outer part of the wall of the optic vesicle and adjacent ectoderm of a 4·5 mm. human embryo. *a*, surface ectoderm; *b*, cavity of optic vesicle; *c*, mitosis near outer surface.

found in the central canal of the spinal cord even in adult life). The outer surface, on the other hand, is very different. The nuclei of the most superficial cells do not come right up to the surface. A narrow margin of protoplasm free from nuclei is left and from this project innumerable small cone-shaped processes. From the apices of the cones come exceedingly fine filaments, which branch and unite with each other and with exactly similar filaments from

Digitized by Illinois College of Optometry Library

rather smaller cone-shaped projections from the cells of the surface ectoderm (as yet only one layer thick) immediately adjacent.

These fibrils can be seen again in Fig. 61, which shews a portion of the wall of the lower part of the same optic vesicle. In this region the fibrils can be seen uniting not only surface and neural ectoderm but also both ectoderms with the vascular mesoderm at the lower margin of the vesicle. The mesodermal cells are rounded and have many protoplasmic processes which unite with the processes from

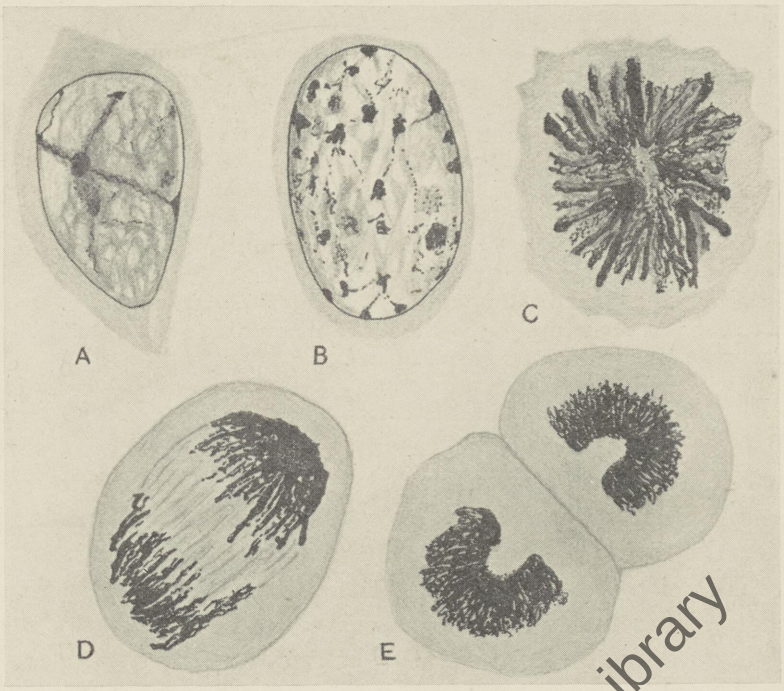


Fig. 60. Five stages of karyokinesis taken from the wall of the optic vesicle of a 4·5 mm. human embryo. *A*, resting nucleus. *B*, early prophase. *C*, metaphase seen from above. *D*, anaphase. *E*, telophase.

the surface cells of the optic vesicle and the surface ectoderm, so that the space between these is crossed by innumerable fine threads and a very definite continuity of protoplasm can be seen between all the structures, both mesodermal and ectodermal, in the neighbourhood. This continuity is quite definite. It has been described by various observers as existing between surface and neural ectoderm (Lenhossek, Magitot) and by von Szily and Wolfrum as existing between ectoderm and mesoderm. By some it has been stigmatised as an artefact, but the fact remains that the fresher and better fixed the material, the more definite do the connecting fibrils appear. It

Digitized by Illinois College of Optometry Library

is also quite compatible with the work of Ranvier, Delépine, Schultze and other physiologists on continuity of protoplasm between cells in the adult.

It has recently been claimed by Dejean that the filaments running between neural and surface ectoderm represent adhesions between two basement membranes which are themselves mesodermal in origin. He claims to have shewn by the use of differential stains on sheep embryos that these adhesions contain collagen and on this assumption declares that they cannot be ectodermal. There are various objections to this theory. In the first place the use of differential staining methods on such early material is extremely unreliable. Such stains depend for their action on differences of chemical composition, that for collagen probably requiring the absence of tryptophane and tyrosin groupings from the protein molecule, and in early embryos complete chemical differentiation has not occurred since practically all the cells are still pluripotential. It seems very doubtful therefore whether the presence of collagen can be held to be provable by staining methods alone. In the second place there is no positive evidence that collagen (or a substance lacking in tryptophane and tryosin) can only be produced by mesoderm during development. We know that it is usually so produced, but we must not forget that mucin, a somewhat similar substance previously thought to be a specific product of ectoderm cells, has now been found in large quantities in cartilage. It seems better to rely on structural appearances of well preserved material than on chemical reactions in such early specimens.

In Fig. 61, as in Fig. 59, the wall of the vesicle is seen to be composed of 8 layers of nuclei. The marginal layer is, however, much better differentiated here than in the upper part of the vesicle. Even at this early stage the region of the future posterior pole of the eye (i.e. the region of the outer wall of the optic vesicle just above and to each side of the insertion of the optic stalk) exhibits the most advanced differentiation. The marginal layer here shews an appearance of definite striation (at right angles to its edge) produced by the cell boundaries. This layer is formed by the clear non-nucleated ends of the most superficial cells of the wall of the vesicle. As in Fig. 59, there are mitoses in the deepest layer and cilia on the basement membrane. The appearance of a marginal layer during differentiation is not confined to the optic vesicle. It occurs all over the central nervous system but at varying times, the optic vesicle and the spinal cord shewing it first (4·5 mm.). Fig. 61 also demonstrates a transient but interesting phase which occurs in the wall of the optic vesicle. At this stage the walls of the whole central nervous system become vascularised by the invasion of fine capillaries, which grow into them from the net of thin-walled vessels which is beginning to cover the surface of the neural ectoderm. This vascularisation occurs on the surface of the optic vesicle as well as over the rest of the fore-brain. It is only seen at the lower part of

Digitized by Illinois College of Optometry Library

the vesicle, since the upper and outer part is still in direct contact with surface ectoderm and practically no vascular mesoderm as yet intervenes. The vascularisation can be quite well seen in Fig. 61. Small capillary spaces, crowded with nucleated foetal erythrocytes, can be seen in the substance of the wall. One of them is almost open on the surface and the continuity of its wall with mesodermal cells outside the vesicle is quite clear. A similar appearance can be seen at intervals all over the wall of the fore-brain. In the fore-brain



Fig. 61. Section through the lower outer part of the wall of the optic vesicle of a 4·5 mm. human embryo. *a*, surface ectoderm; *b*, capillary in wall of vesicle; *c*, vascular mesoderm.

and other parts of the central nervous system it apparently persists and the little capillaries give rise to the definitive vessels of the brain substance, but in the optic vesicle the capillaries only remain until just after the 7 mm. stage. They then disappear entirely and the developing retina is completely avascular until the appearance of the *arteria centralis retinae* at 100 mm. These capillaries crowded with erythrocytes present a very curious appearance and at first sight look like giant cells filled with highly refractile fragments. They have been described by various observers as cells undergoing disintegration. Bach and Seefelder mention them and also state that they may be found half in and half out of the wall of the optic vesicle

Digitized by Illinois College of Optometry Library

and also in the vitreous where they are connected with other cells by protoplasmic fibrils. The impression conveyed is to them that of cells wandering out from the retinal tissue, not, as is probably the case, growing into it from the surrounding mesoderm. Magitot and Mawas also describe them and tend to the view that the fluid of the vitreous is formed by their disintegration. von Szily, however, throws doubt on this, as he is aware that they may be found all over the central nervous system. If they are compared with small capillaries in other parts of the body at this stage, there can be little doubt that the refractile bodies seen in them are red blood cells. It is only to be expected that at this stage, when differentiation of the central nervous system is only just beginning and when growth is extremely active, the optic vesicle should for a time share in the general vascularity. It is interesting also to note that during development the



Fig. 62. Section through the thin portion of the wall of the optic vesicle of a 4·5 mm. human embryo. Note the presence of mitoses and absence of pigment.

retina has two distinct blood supplies, one directly from the surface and transient, the other, appearing much later, from the arteria centralis retinae.

The future outer layer of the optic cup can be recognised at this stage as that portion of the wall of the vesicle which has not thickened. Fig. 62 shews a portion of this. The nuclei are arranged in two or three rows, but it is probable that this appearance is only due to a difference of level and that each cell really stretches from surface to surface. The nuclei nearest the basement membrane (which is ciliated like that of the rest of the central nervous system) shew numerous mitoses, the others are oval with deeply staining chromatin and prominent nucleoli. The cell boundaries can be seen. There is no sign of any pigment anywhere.

Fig. 63 shews the eye of a 5 mm. human embryo. It will be seen that invagination has advanced so that a very definite optic cup, with inner and outer layers, can now be recognised. The marginal

Digitized by Illinois College of Optometry Library

layer is much wider and the protoplasmic cones and strands on its surface are very definitely connected with similar strands from cells of the lens pit. Mesodermal cells and fibrils are beginning to grow between the two and to interlace with them.

Fig. 64 shews a high-power view of a portion of both layers of the cup at its most advanced part. It will be seen that the inner layer is still the same thickness as in Figs. 59 and 61 and shews 6–8 rows of nuclei. (There are still capillaries containing erythrocytes in the

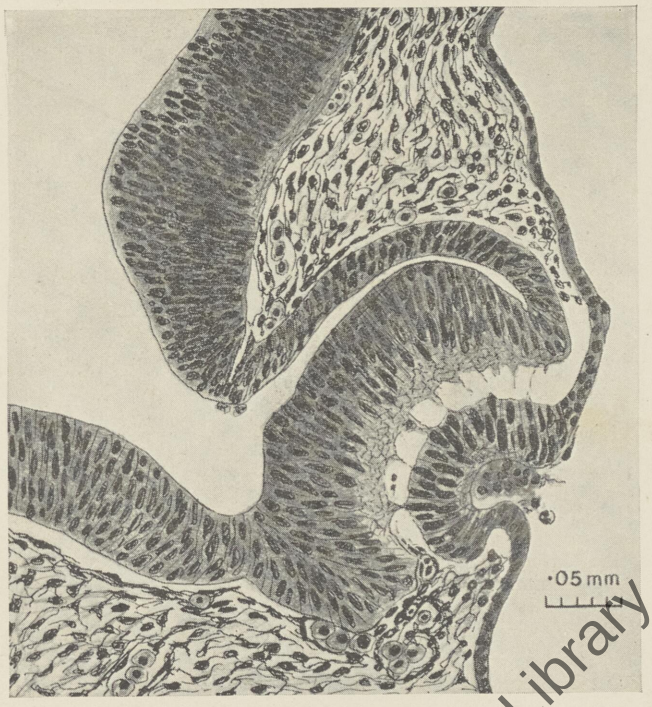


Fig. 63. Section through the optic cup and lens pit of a human embryo of 5 mm.

substance of the inner layer.) There is, however, a slight difference in the appearance of some of the nuclei. In the 4·5 mm. embryo they were all oval; in this embryo one or two on the superficial surface are now round, i.e. differentiation of layers is beginning. There are very few nuclei, smaller than the majority of oval ones, in the marginal layer. In one place there is an appearance of a cell nucleus (probably mesodermal) just passing in at the superficial surface. At another point is seen a protoplasmic cone on which lies one of a little train of vasoformative mesoderm cells which are intruding between retina and lens pit.

The deep or outer layer of the optic cup has much the same

Digitized by Illinois College of Optometry Library

appearance as that seen in Fig. 62. Mitoses are present in both inner and outer walls of the cup, though they are harder to see as this embryo is more darkly stained than the 4·5 mm. There is no trace of pigment.

The next stage for consideration is that shewn by a 10 mm. human embryo. Fig. 65 represents a portion of the inner wall of the cup at the posterior pole. It will be seen at once that the marginal layer

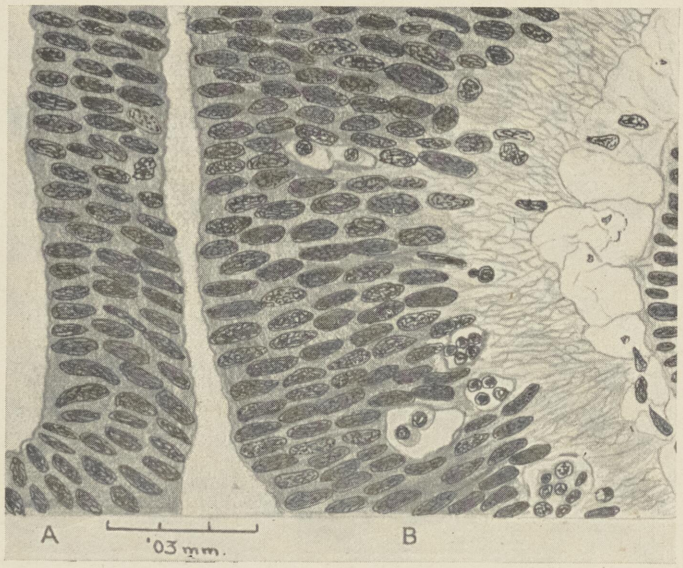


Fig. 64. Section through a portion of the wall of the optic cup of a human embryo of 5 mm. *A*, outer layer of cup. *B*, inner layer of cup.

has increased in width. The thickness as compared with the preceding (5 mm. stage) is:

	5 mm.	10 mm.
a. Total thickness of inner layer of cup	0·07 mm.	0·13 mm.
b. Thickness of marginal layer	0·02 mm.	0·055 mm.
Ratio *b*/*a*	0·28	0·38

Thus we see that there has been an absolute increase in the thickness of both layers as well as a relative increase of the marginal layer. It will also be seen that a few more cells have migrated from the deeper layer into the marginal zone, while a distinct differentiation of cells can be observed. Three main types of cell can now be recognised:

(1) Cells with darkly staining oval nuclei and prominent nucleolus. These are by far the most numerous. They exactly resemble the cells with oval nuclei seen in the previous stage. They are undergoing

Digitized by Illinois College of Optometry Library

mitosis in the deepest layer but not to the extent seen in the 4·5 and 5 mm. specimens. There are still 6–8 rows of them. Some of them take the stain more faintly than others; this may depend on whether they have just divided or not.

(2) Cells with oval nuclei resembling (1). The nuclei stain darkly and the protoplasm of the cell body stains faintly as well (with nuclear stains) and the shape can be made out. These cells are spindle-shaped; they are always arranged with their long axes at

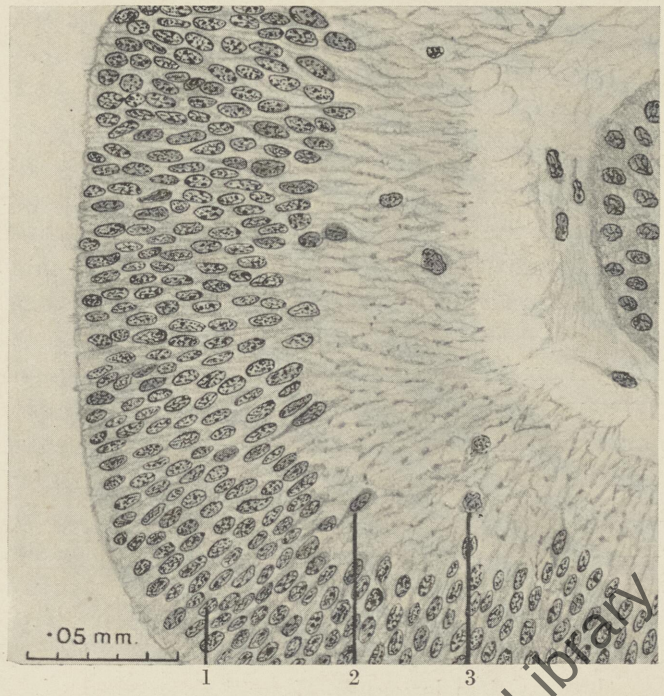


Fig. 65. Section through the inner wall of the optic cup of a 10 mm. human embryo. 1, oval nuclei; 2, spindle-shaped cell; 3, round nucleus (see text).

right angles to the surface of the retina and they possess two long processes, one extending into the marginal layer, but not definitely reaching the surface, and the other passing towards the basement membrane. They are most numerous on the surface of the cellular layer and appear to be passing out of this into the marginal layer. From a study of subsequent stages they can be identified as the first recognisable appearance of the fibres of Müller. Their inner ends have not yet differentiated into "foot plates" and so there is at this time no internal limiting membrane, and the protoplasmic fibrils previously described still pass directly from the surface of the retina into the vitreous. There has been slight shrinkage in this

Digitized by Illinois College of Optometry Library

specimen so that the vitreous net appears in part torn away and retracted from the surface of the retina. It is this appearance of discontinuity which (being common in imperfectly fixed material) has from time to time led to the statement that the retina and vitreous are in no way connected with each other in early stages. An examination of the lateral regions in Fig. 65 will, however, serve to shew that the appearance of a cleft (or, as it has sometimes been described, a lymph space) is an artefact. The early appearance, as distinguishable elements, of the fibres of Müller is in keeping with the general rule of development that supporting tissues are first developed so as to serve as a scaffold around which can be built later the more important and highly specialised tissues. For example, the glial tissue of the marginal layer of the spinal cord appears before the nerve fibre tracts, the optic stalk serves only as a path to conduct the fibres of the optic nerve back to the brain, while the notochord serves as a foundation for the highly specialised vertebral column. In all cases the most highly specialised structures only appear after a foundation has been laid for them by a more simple tissue.

(3) Cells with smaller, round, or very slightly oval nuclei. These are found invariably on either the surface of the layer of oval nuclei (1) or within the substance of the marginal layer itself. They are not at all numerous at this stage and do not form anything like a continuous layer, nor are they found at all except immediately at the posterior pole just above the insertion of the optic stalk. They may be looked on as the earliest of the ganglion cells, but as yet have no processes or other distinctive features save position and alteration of shape of nuclei. They do not possess so distinct a nucleolus as the nuclei in layer (1). It will be noted throughout the histogenesis of the retina that differentiation of the cells is marked by a change in the shape of the nuclei from oval to spherical. This appears to indicate that the cell is losing its power of division, and it can always be taken as the distinction between proliferating and specialising cells. The basement membrane in this specimen shews an irregular edge but definite cilia cannot with certainty be made out. It seems probable that traces of them are present, as they have been seen definitely in other specimens at a later stage.

The outer wall of the optic cup at this stage shews an important change (see Fig. 66). It will be seen that the protoplasm of its cells contains very definite pigment granules. The nuclei still shew many mitotic figures. The boundaries of the cells can be made out and the pigment, which is in the form of minute golden brown dots, is

Digitized by Illinois College of Optometry Library

found in the periphery of the cell, not usually in contact with the nucleus. Traces of cilia are still present on the inner side.

This 10 mm. stage marks the end of what may be arbitrarily described as the first period of retinal differentiation. Up to this time the walls of the optic cup have been seen to be composed of a simple ciliated neuro-epithelium. The outer wall retains this character until almost the end of the period, at which time it is beginning to shew signs of differentiation. These signs take the form of the appearance of pigment granules in the protoplasm of its cells and of disappearance of the cilia which originally covered its inner surface. There is no increase in thickness of this layer either during this stage or indeed throughout life, it remaining always only one cell thick as it was at its first appearance.

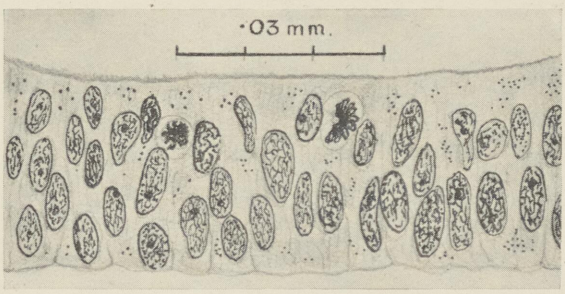


Fig. 66. Section through the outer wall of the optic cup of a 10 mm. human embryo. Note the deposition of pigment granules in the cell protoplasm.

The inner wall of the optic cup (the original outer surface of the optic vesicle) on the other hand shews as early as 4 mm. a very definite increase in thickness. By 10 mm., the end of the first period of development, commencing differentiation into layers is apparent. A nucleus-free *marginal zone* is recognisable, surmounting a *primitive layer* of several rows of cells: these are derived from the division of the original epithelial cells lying against the ciliated basement membrane, which are still visible as the outermost or *proliferating layer*.

As development proceeds, the cells of the proliferating layer continue to divide, both longitudinally and transversely, so that the inner layer of the cup increases at first both in thickness and in area. The increase in thickness continues until the 20 mm. stage, by which time it has reached the adult measurement (0·2 mm.). After this period increase occurs in area only.

Differentiation into layers takes place by the migration of the cellular products of division of the proliferating layer towards the inner surface.

The *primitive layer* of cells resolves itself slowly into two layers

Digitized by Illinois College of Optometry Library

which can be called the *inner neuroblastic layer* and the *outer neuroblastic layer* respectively. The cells of the inner neuroblastic layer, which are more differentiated, have migrated into the marginal layer so that a narrow strip of this last comes to lie between the two primitive neuroblastic layers. This strip is known as the "*transient fibre layer*" of *Chievitz*.

Like the differentiation of the retina in general, this strip is more marked near the posterior pole and varies in definition according to locality.

It is important to remember that it does not represent any recognisable layer in the adult retina, since it disappears completely when growth is finished.

The formation of the layers of the adult retina from the cells of the inner and outer neuroblastic layers takes place by gradual differentiation which extends from the inner to the outer surface. It should be realised that this differentiation proceeds in the inverse direction to the path of the final nerve impulse, the ganglion cells and nerve fibres being the first of the adult retinal elements to appear and the rods and cones the last. The result of this is that, at the time when the percipient elements themselves appear, the layers internal to them are complete and ready to function as conductors immediately.

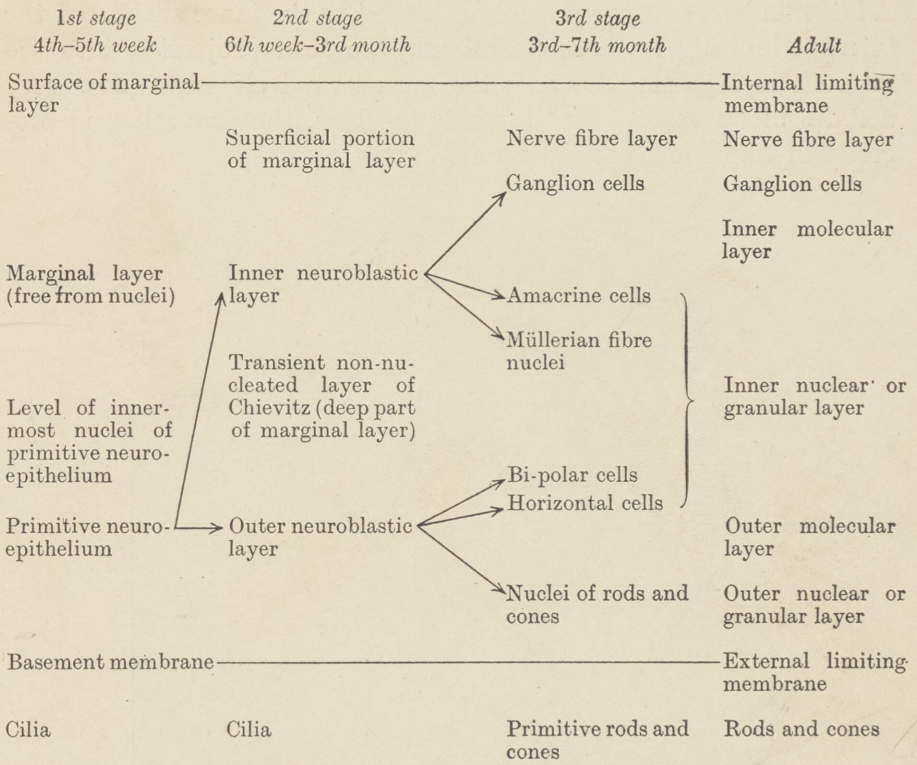
The most superficial cells of the inner neuroblastic layer migrate still further inwards, thus forming another layer, the *layer of ganglion cells*, from which processes grow out to form the nerve fibre layer. The narrow interval remaining between the ganglion cells and the rest of the inner neuroblastic layer becomes the inner molecular layer of the adult retina. The rest of the inner neuroblastic layer differentiates slowly into nuclei of fibres of Müller and amacrine cells.

The cells of the outer neuroblastic layer specialise after those of the inner neuroblastic layer. From them are derived three types of cell. The innermost cells of the layer form *bi-polar cells*, those more external *horizontal cells*, and the outermost the *nuclei of the rods and cones*. A separation, the external molecular layer, becomes apparent between the horizontal cells and the rod and cone nuclei. The final change which takes place is the disappearance of the transient layer of Chievitz and the consequent fusion of the amacrine cells and the nuclei of the fibres of Müller (both derived from the inner neuroblastic layer) with the bi-polar and horizontal cells (from the outer neuroblastic layer) to form the definitive inner nuclear layer or layer of bi-polar cells.

These changes of arrangement of the cells of the developing retina

Digitized by Illinois College of Optometry Library

can be somewhat arbitrarily divided into three periods. The process can be reduced to a tabular form thus:



Such is briefly the outline of the changes which lead to the formation of the retinal layers from the neuro-epithelium of the inner wall of the optic cup. These stages of development will now be illustrated by examples, and the process traced through in detail.

Fig. 67 shews the retina at the posterior pole of the eye of a 12 mm. human embryo. The measurements of the retina are now:

a.	Total thickness of inner layer	0·11 mm.
b.	Total thickness of marginal layer	0·05 mm.
	Ratio *b*/*a*	0·45

Several important differences from Fig. 65 are apparent. There are still on an average eight rows of nuclei, oval, darkly staining and resembling the majority of the nuclei of the preceding stages. The cells of the fibres of Müller, however, are more numerous and obvious. Their nuclei lie in the innermost of the eight rows above referred to, and their inner processes are more easily seen. They run definitely as far as the inner surface and are beginning to spread out on this surface and unite with their fellows, so that an *internal limiting*

Digitized by Illinois College of Optometry Library

membrane is forming and the protoplasmic processes seen in previous stages passing into the vitreous are not now nearly so numerous. A fair number, however, remain attached to the inner surface of the internal limiting membrane and may be seen projecting into the vitreous and passing towards the mesodermal elements (now very definite blood vessels) and towards the lens, the protoplasmic processes of which also are not numerous.

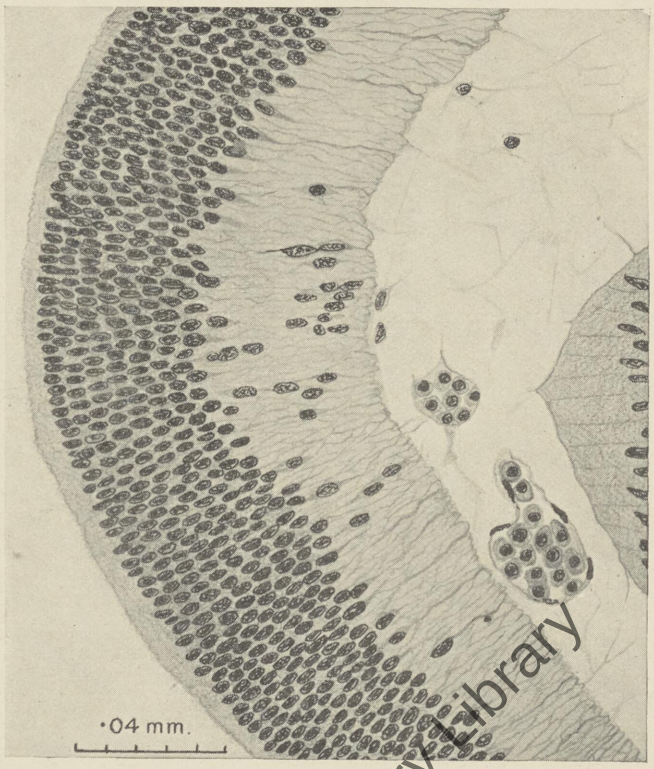


Fig. 67. Section through the inner layer of the optic cup of a 12 mm. human embryo.

Some of the nuclei of the fibres of Müller have migrated into the marginal layer and their outer processes can be seen running back (outwards) towards the proliferating layer. In addition a greater number of cells with rounded nuclei and absence of processes (primitive ganglion cells) are present in the marginal layer but this is only to be seen over one small area, measuring approximately 0·1 mm. horizontally by 0·2 mm. vertically, at the posterior pole. These scattered cells in the marginal layer shew the very beginning of that migration inwards of cells of the primitive neuro-epithelium which leads to the formation of the inner neuroblastic layer in the substance

Digitized by Illinois College of Optometry Library

of the marginal layer. That this inner neuroblastic layer is formed by migration inwards of individual cells and not by a splitting *en masse* of the existing primitive nuclear layer is shewn both by the fact that at its inception the inner neuroblastic layer consists only of a very few cells at the posterior pole (to which are added others, one by one and comparatively slowly) and also by the fact that the width of the marginal layer *plus* the inner neuroblastic layer bears the same ratio to the total thickness of the retina as does the marginal layer alone before the inner layer of cells appears.

The *internal limiting membrane* at this stage (12 mm.) extends in an imperfect state over most of the inner surface of the optic cup except in its extreme lower part, in the region of the choroidal



Fig. 68. Section through the inner surface of the retina and the adjacent vitreous at the lower part of the optic cup of a 12 mm. human embryo. *a*, retina; *b*, vitreous; *c*, mesoderm.

fissure. This region is the newest part of the eye, both ontogenetically and phylogenetically, and differentiation apparently lags behind for a while here. Fig. 68 is a section through the vitreous and the inner surface of the optic cup in this region. It can be seen that the protoplasmic cones and fibrils are extremely well developed (as at the posterior pole in the previous stages, Figs. 64 and 65) and unite very definitely with similar processes from the mesoderm cells entering at the margin of the cup. Foot-plates of fibres of Müller and primitive ganglion cells have not yet appeared in this region.

Fig. 69, however, presents quite a different picture. It is taken from the margin of the cup at the same level as Fig. 67. This section is chosen on account of the fact that slight shrinkage has taken place at the margin, leading to a tearing away of the internal limiting membrane from the retina. The fact that when shrinkage occurs,

Digitized by Illinois College of Optometry Library

as it does with great frequency in older material, the internal limiting membrane tears away from the retina and remains in continuity with the vitreous, is a further proof, if one were needed, of the intimate connection between vitreous and retina. There is never anything to be seen in embryonic stages to warrant the assumption that a hyaloid membrane separating the vitreous from the retina exists apart from the internal limiting membrane which itself appears to be in continuity with the two. In Fig. 69 the foot-plates of the fibres of Müller are easily seen forming by their union a continuous membrane, to the outer side of which are attached the fibres of

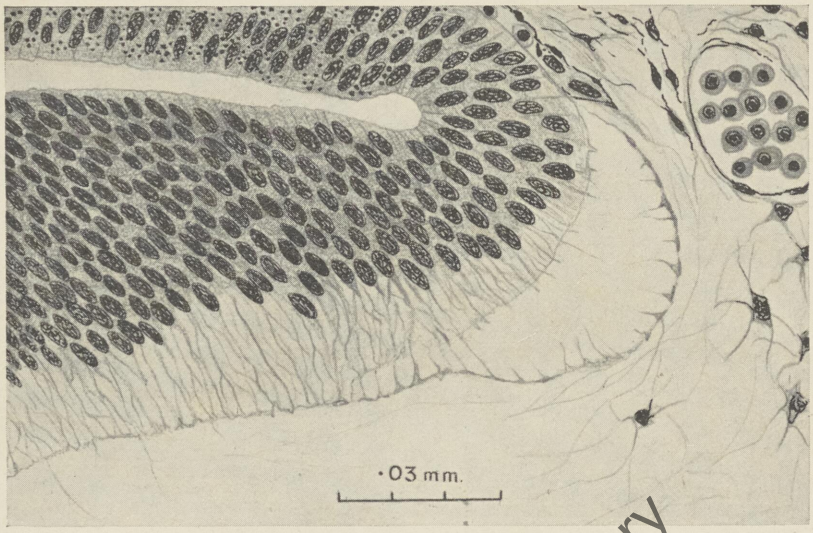


Fig. 69. Section through the margin of the optic cup of a 12 mm. human embryo.

Müller themselves and to the inner side the ectodermal fibrils of the vitreous, blending with processes from the mesodermal cells at the margin of the cup.

With regard to the general statement often made that the periphery of the cup at a given age resembles in stage of differentiation the central region at an earlier age, it should be noted that Fig. 69 affords a good example of just how far this principle can be carried. The inner layer at the margin of the cup certainly resembles that seen in Fig. 64 in that it consists of 6–8 rows of oval nuclei and a clear marginal layer. It differs, however, from the earlier stage in two important particulars, namely that fibres of Müller and an internal limiting membrane are present and that pigment is developed in the outer wall of the cup in contact with it. The resemblance is thus superficial only and is seen to fall short when examined in detail.

Digitized by Illinois College of Optometry Library

Differentiation proceeds rapidly at the region of the posterior pole, and Fig. 70 shows how definite is the appearance of the inner neuroblastic layer in a 17 mm. human embryo. The whole eye is shewn. The inner and outer walls of the cup are separated by a wide space, the remains of the cavity of the primary optic vesicle. The section

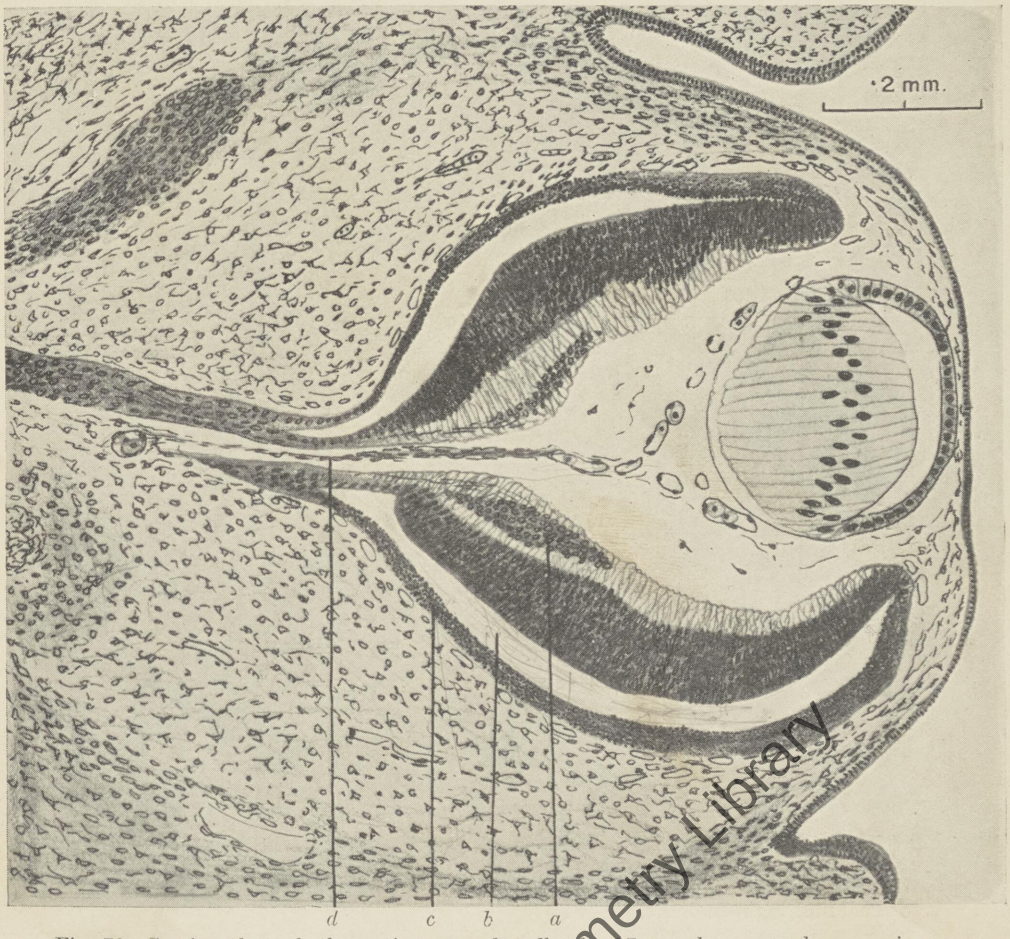


Fig. 70. Section through the optic cup and stalk of a 17 mm. human embryo. *a*, inner layer of cup with inner neuroblastic layer; *b*, cavity of primary optic vesicle; *c*, outer pigmented wall of cup; *d*, hyaloid artery in upper end of foetal fissure.

passes longitudinally through the optic stalk, and the extreme upper end of the foetal fissure with the hyaloid artery entering it and branching in the vitreous can be seen. The single layered epithelium of the stalk and outer wall of the cup is in sharp contrast with the thickness and complexity of the inner wall. Over the whole extent of the inner wall, except just at the growing rim of the cup, the clear marginal layer, bounded internally by the internal limiting

Digitized by Illinois College of Optometry Library

membrane, is well developed. On either side in the region of the entering hyaloid artery this marginal layer is very sharply divided into two by a mass of cells lying in it (in the situation of the scattered cells seen in Figs. 65 and 67). Some of these cells are ganglion cells and are at this stage giving origin to definite dendrons which can be seen running in the scaffolding of the non-nucleated marginal layer, at

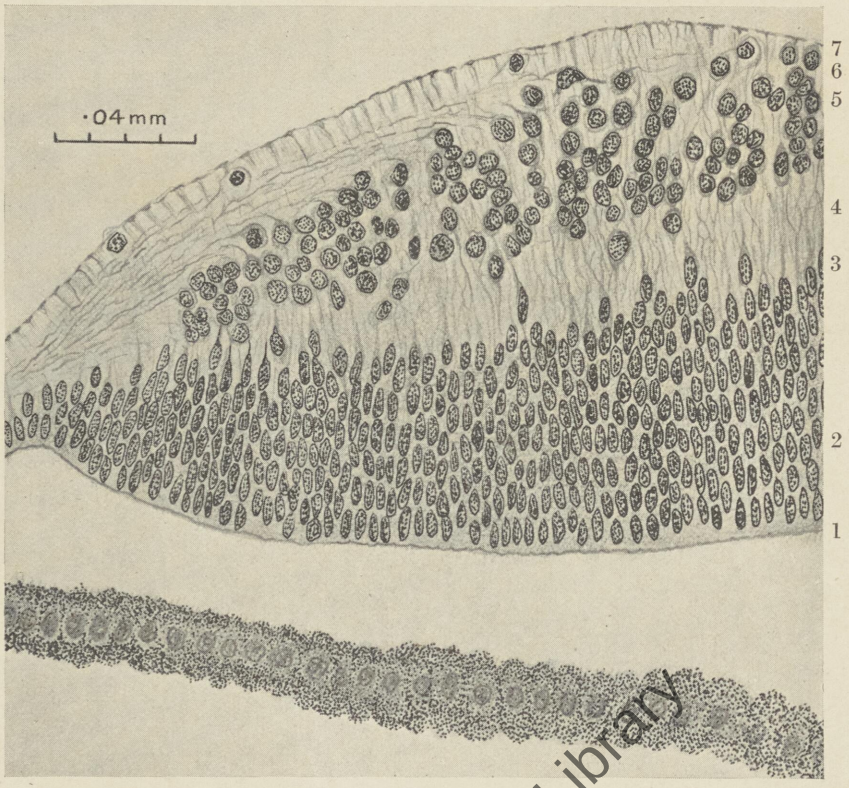


Fig. 71. Section through the retina in the region of the inner neuroblastic layer (from the eye shewn in Fig. 70—17 mm. stage). 1, basement membrane; 2, outer neuroblastic layer; 3, fibres of Müller; 4, layer of Chievitz; 5, inner neuroblastic layer; 6, nerve fibre layer; 7, internal limiting membrane.

right angles to its fibres, towards the upper end of the foetal fissure, in order to reach and run centripetally in the inner layer of the optic stalk. This is the first appearance of nerve fibres in the eye or optic nerve. They can be traced along the under surface of the optic stalk almost to the brain at this stage.

Fig. 71 shews a high-power drawing of the region of the inner neuroblastic layer seen in Fig. 70.

The following structures can be seen in the inner wall from the outer margin inwards:

Digitized by Illinois College of Optometry Library

(1) Basement membrane with protoplasmic veil of cilia.

(2) Six or seven rows of oval nuclei, their long axes at right angles to the basement membrane, and all resembling in type and arrangement the nuclei of the proliferating layer in the earlier stages, save that mitoses are now much harder to find.

(3) Cells with their oval nuclei on the surface of this layer and also occurring in the next layer (4). They have inner and outer processes, i.e. they are fibres of Müller. The inner and outer processes of these cells pass up to the inner surface and expand into foot-plates, the union of which forms the internal limiting membrane now to be seen very definitely on the surface of the retina.

(4) A clear layer, filled with the inner processes of the fibres of Müller and containing a few of their nuclei. This is the transient fibre layer of Chievitz and was the outermost portion of the marginal zone before the nuclei of the inner neuroblastic layer migrated inwards.

(5) Inner neuroblastic layer. The cells of this layer are rapidly differentiating and the most superficial of them shew a definite cell outline, with one, two or three processes. These are ganglion cells. One process, the dendron, passes horizontally into the 6th layer. Their nuclei are round with a deeply staining chromatin net. The more deeply situated cells of this layer do not shew the characteristics of ganglion cells but are undifferentiated. Some of them form ganglion cells, others amacrine cells at a later period. This early appearance of distinguishable ganglion cells at the same time or even a little before the growth of nerve fibres towards the optic stalk is of importance, since many observers in the past have advanced the theory that the fibres of the optic nerve were central in origin and that they grew from the brain towards the eye during development. A study of the retina at this stage serves to shew beyond a doubt that they arise from the ganglion cells of the retina and extend centripetally. This view is amply corroborated by degeneration experiments, which however bring out the fact that there are also a few centrifugal fibres of smaller calibre present in the adult optic nerve. Their embryonic origin has not yet been successfully demonstrated.

(6) The sixth layer consists of a network of longitudinal and transverse fibres. The fibres running at right angles to the surface (transverse) are the more numerous and they alone are present in the most superficial region. They are fibres of Müller. The longitudinal fibres can be traced to the cells of the 3rd layer on the one hand and into the inner layer of the optic stalk on the other. They

Digitized by Illinois College of Optometry Library

are the nerve fibres of the optic nerve, but as yet they do not fill the space provided for them. The whole retina is bounded internally by

(7) The spread out and united ends of the fibres of Müller (internal limiting membrane).

The inner wall of the optic cup at the posterior pole measures at this stage 0·175 mm. in thickness, while the marginal layer, *plus* the inner neuroblastic layer which it contains, measures 0·08 mm. Comparison of these measurements with those of the earlier stages makes it appear probable that the inner neuroblastic layer is formed by migration of nuclei into the marginal layer and not by a splitting of the original nuclear layer, since, though an absolute increase in thickness of the marginal layer has taken place with the appearance of the ganglion cells, the ratio between the thickness of the marginal layer and the total thickness remains unchanged.

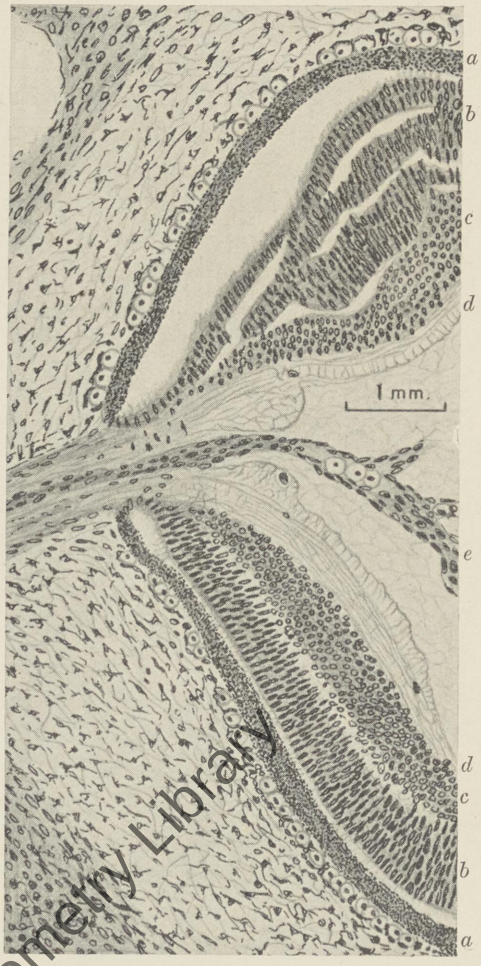


Fig. 72. Section through the posterior pole of the eye of a 21 mm. human embryo. *a*, outer layer of optic cup; *b*, outer neuroblastic layer; *c*, inner neuroblastic layer; *d*, nerve fibre layer *e*, hyaloid artery.

The outer wall of the optic cup (Fig. 71) shews that the nuclei are arranged in a single row and that the pigment has increased in amount so that the granules completely fill the cell. The pigment grains in the outer wall of the cup are from the beginning spherical in shape in man. In many of the lower animals they are in the form of needles, crystals, or small rods, and are constant for the species.

Fig. 72 shews a section through the posterior part of the eye of a 21 mm. human embryo. It will be seen that the inner layer of cells which had separated from the deep layer in the previous stage is now thicker and greater in extent. Fig. 73 shews a portion of this region seen under a higher power. Certain differences have

Digitized by Illinois College of Optometry Library

occurred since the 17 mm. stage. Considering the layers *seriatim*, one finds:

(1) The outer limiting membrane of the inner wall of the cup, which up to the present has been visible and has given the impression of being covered with short and ill-developed cilia, now appears irregularly serrated in outline, and gives origin to much longer filaments: these are further apart and definitely reaching across the remains of the cavity of the primary optic vesicle to touch the outer pigmented wall of the cup. These fine filaments appear to be an early stage of the little protoplasmic projections which appear outside the external limiting membrane in the next stage and finally differentiate into the rods and cones. The filaments seen at the 21 mm. stage can be taken to represent the outer limbs of the rods, which arise before the inner limbs. (The vesicular swellings which appear at the origin of the outer limbs from the external limiting membrane, at the next stage, represent the inner limbs.)

(2) The 6–7 rows of oval nuclei seen as the second layer (outer neuroblastic layer) in the previous stage (Fig. 71) are still present unchanged in shape, number and arrangement. Mitoses may still occasionally be found in the deepest row, but this is more common at the periphery of the retina than at the posterior pole.

(3) A narrow interval, the transient fibre layer of Chievitz, crossed by fibres of Müller, intervenes between the most superficial of the oval nuclei and the next nuclear layer.

(4) This layer (inner neuroblastic layer), though it appears more or less homogeneous under a low power, shews signs when more carefully examined of dividing into two. It is 8 cells thick. The more deeply placed 5 or 6 rows of nuclei shew transition in shape from below upwards from oval to round in outline, pointing to the probability that they are forming by differentiation of the nuclei of layer 2 above. These 5 or 6 rows of transitional nuclei do not stain so darkly as the rest and their chromatin often assumes a radial arrangement in the nucleus. Certain of the oval nuclei may often be seen to be connected with

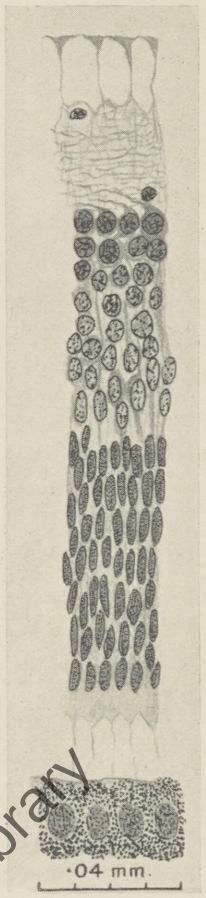


Fig. 73. Section through a portion of the retina seen in Fig. 72. 1, rudiments of rods and cones; 2, outer neuroblastic layer; 3, layer of Chievitz; 4, inner neuroblastic layer; 5, nerve fibre layer; 6, internal limiting membrane.

Digitized by Illinois College of Optometry Library

fibres of Müller. The most superficial 2 or 3 rows of nuclei shew the characteristics of ganglion cells similar to those seen in the previous specimen (Fig. 71). Thus we see that this layer of cells can be divided

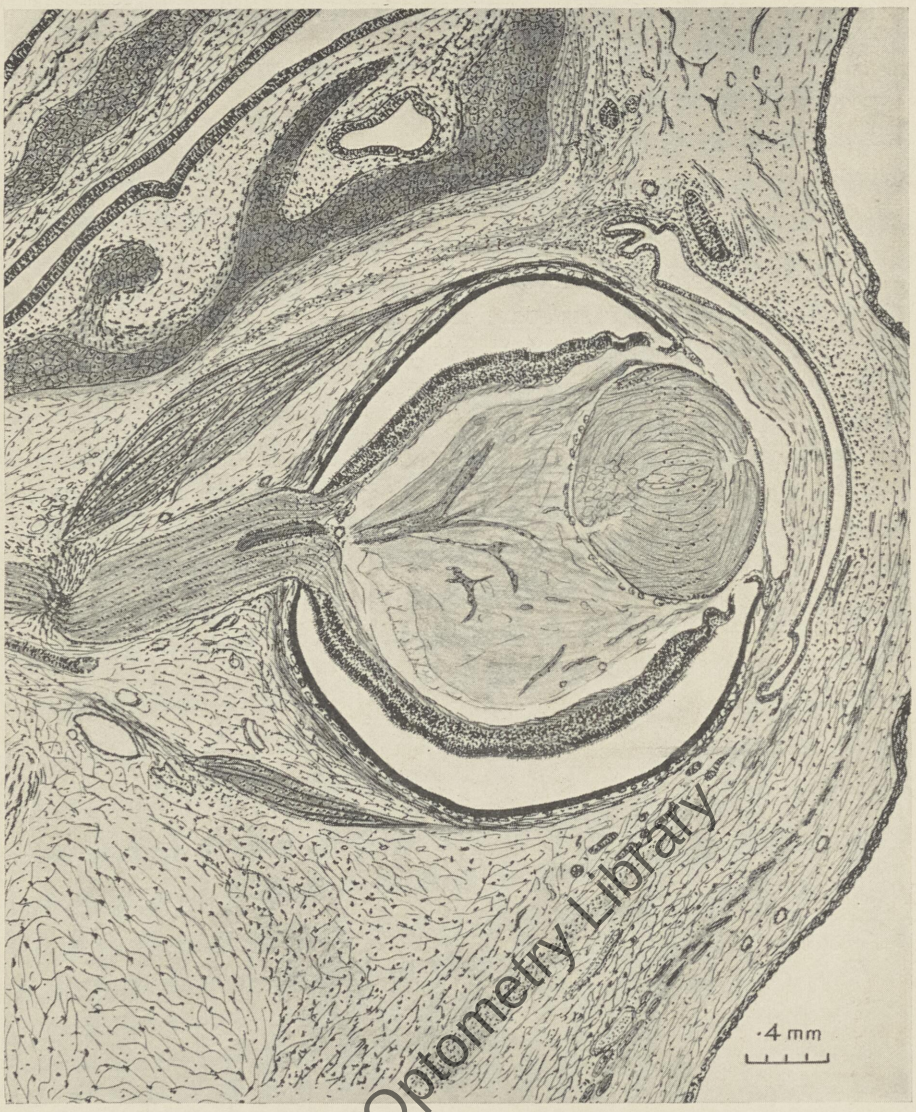


Fig. 74. Section through the eye and orbit of a 48 mm. human embryo.

into two. The superficial set is destined to become ganglion cells and the deeper set will further differentiate into nuclei of fibres of Müller (already recognisable) and nuclei of amacrine cells.

(5) The layer of nerve fibres from the ganglion cells can be seen to be considerably thicker, though there is still a wide interval be-

Digitized by Illinois College of Optometry Library

tween the most superficial of the nerve fibres and the internal limiting membrane—in other words, the glial scaffolding is not yet all filled up.

The outer pigmented wall presents very much the appearance of the same layer in the adult save that the pigment is not so dense. The measurements of the layers are:

a.	Total width of inner wall of optic cup	0·19 mm.
b.	Width of original marginal layer now containing ganglion cells, amacrine cells and nuclei of fibres of Müller	0·11 mm.
	Ratio *b*/*a*	0·57

The ratio *b*/*a* is now 0·57, shewing that there has been a slight relative as well as an absolute increase in the thickness of the original marginal layer, which now, of course, contains the inner neuroblastic layer of nuclei.

The next stage for examination, the 48 mm. embryo, of which the whole eye and orbit is seen in Fig. 74 and a portion of the retina in Fig. 75, shews the further subdivision of the cell layers.

The inner neuroblastic layer has definitely split into a ganglion cell layer and a layer of supporting and amacrine cells, while the outer neuroblastic layer is beginning to shew a distinction between nuclei of visual elements and nuclei of bi-polar cells. The layers at the posterior pole will, as before, be described from without inwards.

(1) The external limiting membrane. As in the previous stage, long filaments of protoplasm pass from this towards the pigment layer. In addition the proximal end of each filament appears swollen (and occasionally beaded) as if the filament arose from the summit of a little cone-shaped vesicle of protoplasm projecting from the cell. These little cones (which are foreshadowed in Fig. 73) are the earliest signs of the inner limbs of the visual elements.

(2) At the same time that these protoplasmic cones appear the nuclei immediately adjacent to them undergo differentiation. Mitoses can now no longer be seen in them, they lose their oval form and become round and often kidney-shaped[1] and form a definite layer (2) marked off from the stratum of oval nuclei (3) above them. As soon as this happens no more mitoses can be seen in this portion of the retina. The cells in it have reached their full number and only

[1] These round and kidney-shaped nuclei probably represent nuclei of cones. They appear first in the region of the posterior pole where cones are always more numerous, and their position, just alongside the external limiting membrane, corresponds with the final position of the cone nuclei. The nuclei of the rods, which finally lie more deeply in the outer nuclear layer, are probably derived from the outermost of the oval nuclei of the next layer (3).

Digitized by Illinois College of Optometry Library

undergo differentiation and re-arrangement. Increase in size of the retina occurs from now onwards by thinning of the nuclear layers, with corresponding increase in width of the fibre layers, and by increment from the as yet undifferentiated equatorial and peripheral regions.

(3) The layer of oval nuclei. What was previously the deepest layer of these has, as noted above, now differentiated, forming nuclei of cones. There still remain seven tiers of oval nuclei above this. They shew no distinction as yet into nuclei of rods and nuclei of bi-polar cells.

(4) The next layer (which is separated from 3 by the narrow transient layer of Chievitz) is composed of 15–18 tiers of nuclei in its thickest part. They are round in outline, rather more faintly staining than the cells of layer 3, and shew the same radial arrangement of chromatin seen in the corresponding cells in the 21 mm. specimen (Fig. 73). The differentiated ganglion cells, which in the 21 mm. embryo formed the most superficial tiers of this layer, are now separating and are present as a rather irregular layer (5) embedded in the nerve fibre layer (6). Further increment of ganglion cells occurs by differentiation of the most superficial cells of layer 4, which migrate inwards. Cells in passage from the 4th layer to the 5th can be seen.

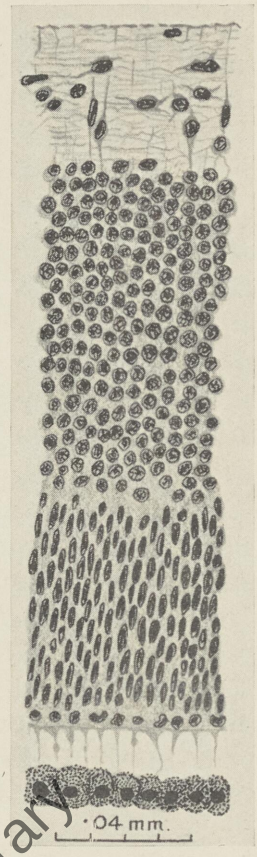


Fig. 75. Section through the retina of a 48 mm. human embryo. 1, external limiting membrane; 2, kidney-shaped nuclei; 3, outer neuroblastic layer; 4, nuclei of bi-polar and amacrine cells; 5, ganglion cells; 6, nerve fibre layer.

(5) In the 5th layer the ganglion cells are the most superficial and deep to them and in places blending with the nuclei of layer 4 are the nuclei of the fibres of Müller.

(6) The nerve fibre layer extends up to the internal limiting membrane, which can still be easily recognised with the foot-plate of the fibres of Müller forming it.

This stage is important as it marks the first appearance (at the posterior pole), at and around the region of the future macula, of the beginnings of the visual elements themselves. Indeed in this area all the components of the adult retina can be recognised, though as yet in rudimentary form. The cells, with their protoplasmic cones

Digitized by Illinois College of Optometry Library

projecting beyond the external limiting membrane and their kidney-shaped nuclei against the membrane, represent the first neuron of the afferent path. The oval nuclei superficial to these represent the bi-polar cells, or second neuron, and the ganglion cells the third neuron along which the impulse passes back to the brain.

The amacrine cells and the nuclei of Müllerian fibres of layer 4 appear as a separate layer only transiently. They become blended with those of the layer beneath (3) to form the inner granular layer (bi-polar layer) later.

The origin of the outer and inner limbs of the rods and cones deserves further consideration at this stage. That they appear as protoplasmic protrusions in the region of the external limiting membrane is undoubted. Graham Kerr, from observations on lower forms, states that the external limiting membrane is bulged before them as they develop and that they carry a thin covering of this as far as the junction of their inner and outer limbs. One must remember, however, in following discussions on this point, that the term "external limiting membrane" is often used loosely for two rather different structures. Here and in the writings of most embryologists it is taken to mean the outermost edge of the cells of the proliferating layer. It must not be forgotten, however, that, later, the fibres of Müller extend to this outer edge and form by the union of their outer processes a membrane resembling the internal limiting membrane but more delicate and richly fenestrated. From the protoplasmic nature of the inner limbs of the rods and cones it is obvious that they must carry with them a covering derived from the original cell boundary (embryonic external limiting membrane) from which they are an outgrowth, and since they appear before the growth of the outer processes of the Müllerian fibres it seems equally certain that they derive no covering from the definitive external limiting membrane, but simply come to protrude through its fenestrations when these are formed later around their bases. The appearance of the region of the external limiting membrane (i.e. a very definitely ser rated edge) in Figs. 73 and 75 certainly appears to bear this out and it is certain that the inner limbs are definitely protoplasmic and not in the nature of a cuticular secretion.

The question now arises—can the outer limbs be identified with the cilia which originally lined the cavity of the central nervous system? It has been seen by the foregoing diagrams that it is almost impossible to say that the original cilia disappear, leaving an interval of time before the appearance of the rod and cone outgrowths, during which the external limiting membrane exists as a smooth basement

Digitized by Illinois College of Optometry Library

membrane. In the earliest embryos the cilia are quite definite, lining the cavity of the primary optic vesicle and the cavity of the fore-brain. From thence onwards traces of them can always be seen, sometimes as definite short hair-like processes and sometimes merely as a sort of indefinite veiling of the surface by a faintly staining band. The appearance offered by different specimens appears to depend much more on the state of preservation of the embryo than on its age. In all cases up to the 21 mm. stage the appearance of the lining of the cavity of the brain and the central canal of the spinal cord was exactly similar to that of the external limiting membrane of the retina. At 21 mm., although cilia can be seen in the cavity of the fore-brain, the processes from the retina are definitely longer and more widely separated than before and can be looked on as beginnings of the outer limbs of the rods and cones. They thus would seem to arise by increase in size and reduction in number of pre-existing cilia. Whether or not this is the case is difficult to determine since the structures involved are so delicate and so liable to give rise to artefacts during preparation. It is, however, worthy of note that while an appearance of cilia can be seen continuously on the inner wall of the optic cup, the outer wall cells very definitely lose them soon after the development of the pigment granules. One is therefore safe in drawing at least a close parallel if not a definite derivative relation between cilia and the primitive outer limbs of the visual elements.

The pigment layer of the 48 mm. embryo is unchanged. It shews no trace of cilia, the nuclei are arranged in a single row and the cells are full of pigment.

The next stage for consideration is that seen in a 0·65 cm. human embryo. Fig. 76 shews the whole eye of this embryo under a low power. It is at once evident that differentiation is far advanced and that the whole eye and surrounding region has now come to resemble the adult organ very closely except in size.

Fig. 77 shews a more enlarged view of a portion of the retina from the posterior pole of the eye. The layers to be recognised are, from without inwards:

(1) The layer of rudimentary outer and inner limbs of the rods and cones, bounded internally by the external limiting membrane. The inner limbs project from this as protoplasmic cones of varying sizes, from the apices of which the outer limbs arise as fine threads, passing towards the pigment layer.

(2) The layer of cone nuclei. These now form a single layer of spherical nuclei separated by a narrow space from the layer of in-

Digitized by Illinois College of Optometry Library

different oval nuclei (3). (It is to be noted that this space does *not* represent the external molecular layer.)

(3) A layer consisting of 6 tiers of oval nuclei. The inner of these nuclei are taking on a spherical shape and are blending with the next cell layer. Between the two layers is a gap filled by fibrils

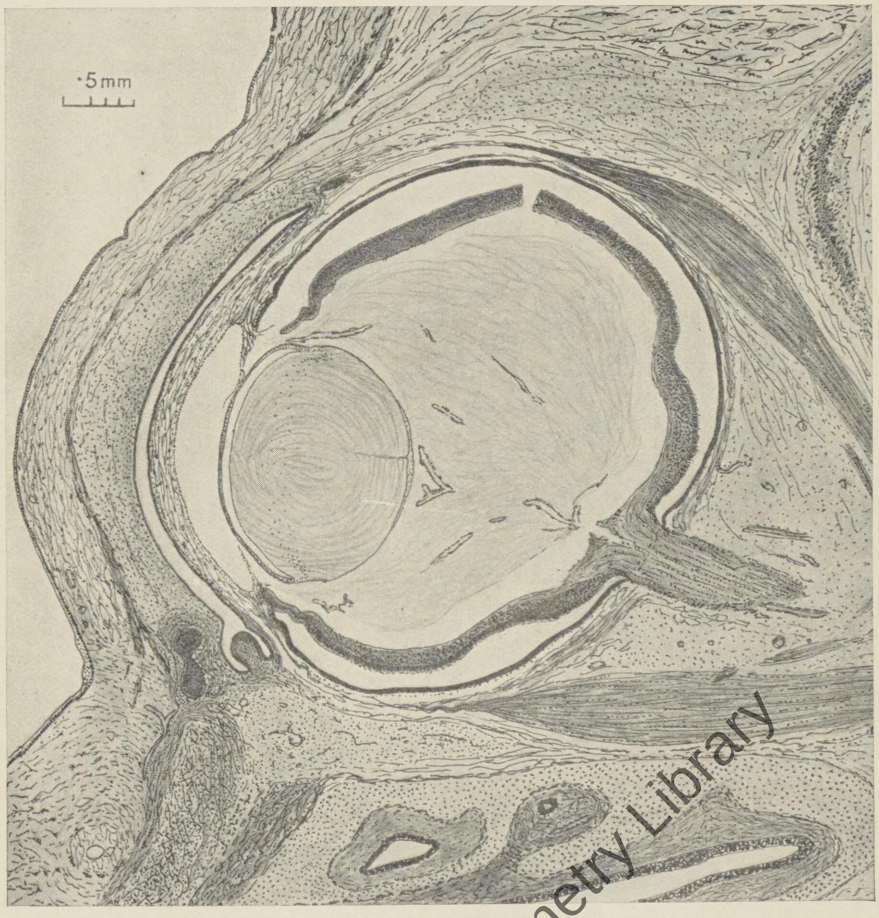


Fig. 76. Section through the eye and orbit of a 3 months foetus.

(layer of Chievitz) but it is not a complete gap, as many round nuclei appear to have wandered into it. This layer of Chievitz can be recognised all over the retina as the line of transition between the round and the oval nuclei. It is only on the temporal side, in the region of the future macula, that it attains a definite thickness. The general impression given by this specimen is that of cells migrating inwards as their nuclei differentiate.

(4) The layer of mixed nuclei (amacrine cells and fibres of Müller).

Digitized by Illinois College of Optometry Library

This now contains some 6–10 tiers of nuclei. They are faintly staining, with radially arranged chromatin and are more widely separated from each other than in the 48 mm. specimen. The deepest ones resemble the most superficial ones in the layer below, and are in places continuous with them. The most superficial in this layer (4) are connected with fibres of Müller. This layer is now more definitely separated from the layer of ganglion cells by a layer of fibrillar structure, the future inner molecular layer.

(5) The layer of ganglion cells. These have much the same appearance as those seen at 48 mm. but are more numerous and more evenly arranged.

(6) The layer of nerve fibres completely fills the space between the ganglion cells and the internal limiting membrane.

The pigment epithelium has undergone but little change save that the pigment is now so dense that the nuclei of the cells cannot be seen in unbleached specimens.

The actual measurements of the layers are as follows:

a. Total thickness of inner wall of cup	0·143 mm.
b. Thickness of original marginal layer	0·08 mm.
Ratio *b*/*a*	0·55

The difference in thickness of the layer of amacrine cells in this specimen and that of 48 mm. appears to be definitely correlated with the increase in surface area of the whole retina.

The stage of differentiation seen in Fig. 77 is only found at the posterior pole.

In the anterior equatorial region the picture presented is that seen in Fig. 78. This shews an arrangement which at first sight might be thought to be typical of the posterior pole at an earlier stage, for example, the 21 mm. embryo (Fig. 73), since only two layers of nuclei, the inner round and the outer oval, are seen. Closer comparison of the two specimens will shew however, that the resemblance is only superficial.

In the 65 mm. embryo (Fig. 78) the basement membrane is seen with a few indefinite processes resembling degenerating cilia protruding from it. Internal to this are seen the cells of the proliferating layer, still with numerous mitoses (since at this stage increase in size of the retina is brought about by growth of the periphery only). Internal to these dividing cells are 8 tiers of oval nuclei and internal to these again are 8–9 tiers of round nuclei, the line of transition from the one to the other marking the level of the fibre layer of Chievitz, here not recognisable as a layer at all. Between them and

Digitized by Illinois College of Optometry Library

the internal limiting membrane is a narrow space (the marginal layer) crossed by the fibres of Müller and shewing here and there a few longitudinal fibrils but no ganglion cells and no unmistakable nerve fibres.

On the other hand, the 21 mm. specimen shews already differentiating ganglion cells, a wider marginal layer, and the beginning of

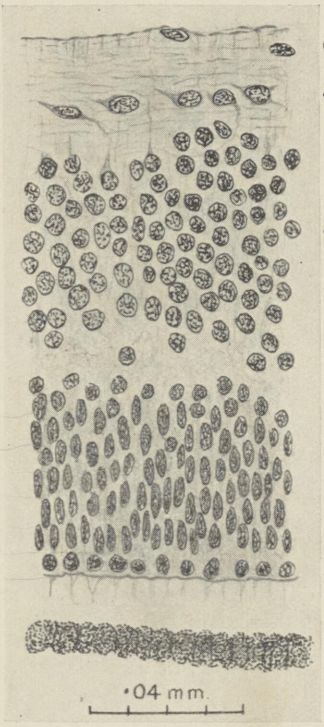


Fig. 77. Section through the retina at the posterior pole in a 65 mm. human embryo. 1, primitive rods and cones; 2, cone nuclei; 3, oval nuclei (undifferentiated); 4, amacrine nuclei and nuclei of fibres of Müller; 5, ganglion cells; 6, nerve fibre layer.

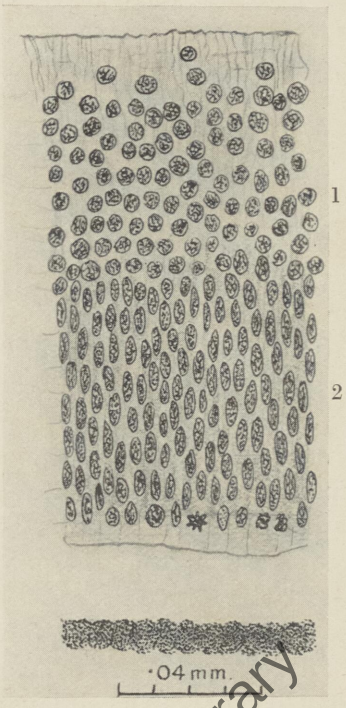


Fig. 78. Section through the retina in the anterior equatorial region of the eye of a 65 mm. human embryo. 1, round nuclei (inner neuroblastic layer); 2, oval nuclei (outer neuroblastic layer).

primitive visual elements. Thus the resemblance holds good only in that there is separation into two main zones of cells (outer and inner neuroblastic layers) in both.

At the 4th month (110 mm.) can be demonstrated for the first time the position of the future outer molecular layer.

Fig. 79 shews a section through the retina near the posterior pole at this stage. It will be seen that an irregular layer of cells with round nuclei can be made out among the oval nuclei of the inner

Digitized by Illinois College of Optometry Library

layer. There is not a definite dividing space between the nuclei of the rods and cones and the bi-polar nuclei, but these round nuclei mark the position where this will occur. The nuclei themselves are those of the "horizontal cells" found in the adult retina at the outer edge of the layer of bi-polar cells. In some fishes (e.g. *Amia calva*) these cells are arranged in a very definite single row, but in the human retina they are more scattered. Internal to these lie the rest of the oval nuclei (now earmarked as bi-polar cell nuclei) which form a layer entirely continuous with the layer of amacrine cells on their inner aspect. Thus, at this stage, the transient fibre layer of Chievitz seen between the amacrines and the oval nuclei in the stages before this has disappeared (except at the macula, where it persists until after birth). Internal to the amacrine cells again lies the now definite but narrow fibre layer (inner molecular layer) which separates them from the ganglion cells. These latter, together with the inner limbs of the fibres of Müller and the nerve fibre layer proper, can be recognised easily. The ganglion cell layer at the posterior pole is now 4–6 cells thick.

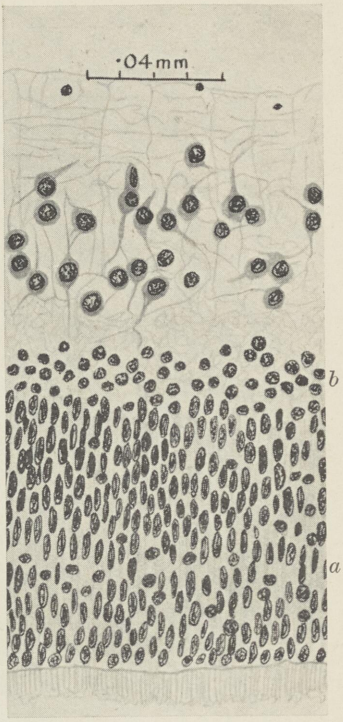


Fig. 79. Section through the retina of a 110 mm. foetus; *a*, level of horizontal cells and external molecular layer; *b*, level of layer of Chievitz in earlier stages.

The measurements of the retina at this stage are:

a.	Total thickness of inner wall of optic cup	0·165 mm.
b.	Thickness of original marginal layer (see Fig. 79)	0·09 mm.
	Ratio *b*/*a*	0·54

so that we see that only a very slight actual increase in thickness has occurred since the 65 mm. stage, while the relative width of the two components remains the same.

A further stage in the separation of the nuclei of the rods and cones from the bi-polar nuclei (i.e. the formation of the external molecular layer) can be seen in Fig. 80. This shews the retina near the posterior pole in a foetus of $5\frac{1}{2}$ months (170 mm.). It will be seen that all the layers found in the adult are present and bear the

Digitized by Illinois College of Optometry Library

final relation to each other, though their differentiation is not yet complete. From without inwards the layers are:

(1) Layer of rods and cones. This specimen was not sufficiently well preserved for these elements to be seen in detail but they are larger than in the preceding stage.

(2) External limiting membrane. This is now very well marked and definite. The outer processes of the fibres of Müller have reached the original basement membrane and now form the definitive fenestrated external limiting membrane.

(3) Layer of nuclei of rods and cones. These now form a layer, 5–7 rows deep, bounded on its inner side by a narrow space, the external molecular layer. The nuclei nearest the external limiting membrane are presumably cone nuclei, the others those of the rods. The distinction is not very clear, though the cone nuclei tend to appear spherical, the rod nuclei oval.

(4) External molecular layer. A few round nuclei can be found in this layer; they appear to be nuclei of horizontal cells which are in process of passing into the 5th layer.

(5) Layer of bi-polar cells. This layer in reality contains four types of cell, i.e. the amacrine cells, the bi-polar cells themselves, the nuclei of the fibres of Müller and the horizontal cells. It is formed, as will be seen by a comparison with the previous stages, by the fusion of the layer of amacrine cells and nuclei of Müllerian fibres (which were originally derived from the *inner* neuroblastic layer) with the innermost 7–8 rows of nuclei of the original *outer* neuroblastic layer (bi-polar and horizontal cells). The *amacrine* cells have spherical nuclei and lie on the surface of the layer; the *bi-polar* cells have also by this stage mostly spherical nuclei, which stain darkly. The *nuclei of the Müllerian fibres* can be distinguished as the rather large and oval ones, lying among these bi-polars, and inner and outer processes can be seen attached to them.

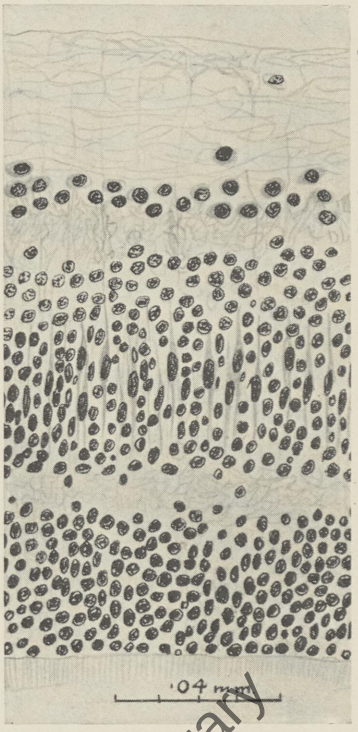


Fig. 80. Section through the retina near the posterior pole in a foetus of 170 mm. 1, rods and cones; 2, external limiting membrane; 3, nuclei of rods and cones; 4, outer molecular layer; 5, inner granular layer; 6, inner molecular layer; 7, ganglion cells; 8, nerve fibre layer; 9, internal limiting membrane.

Digitized by Illinois College of Optometry Library

The *horizontal* cells form an irregular row of round nuclei rather more faintly stained than those of the bi-polar cells and lying on their outer side.

(6) The inner molecular layer. This is quite definite, but still narrow.

(7) Layer of ganglion cells. This is still 2–3 cells thick.

(8) Nerve fibre layer. It appears somewhat oedematous in the specimen drawn, but this is probably an artefact.

(9) Internal limiting membrane.

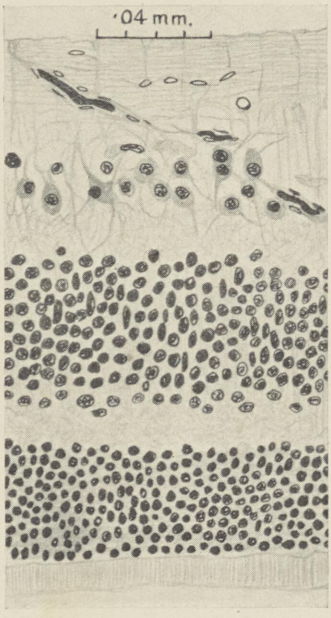


Fig. 81. Section through the retina in the para-central region of a 250 mm. foetus.

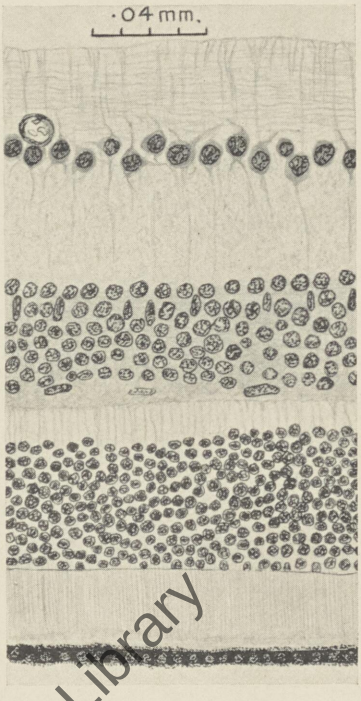


Fig. 82. Section through the adult human retina.

By 7 months the retina has assumed practically the adult arrangement and proportions. Fig. 81 shews the para-central region in a 7 months foetus (250 mm.) in which the carotid had been injected with Indian ink. The blood vessels can be seen vascularising the inner layers. At this stage none of the nuclei of the outer granular layer (rod and cone nuclei) retain their primitive oval shape. They are all differentiated. In the inner nuclear layer oval nuclei are seen at intervals, but these are the nuclei of the fibres of Müller, all the rest in this layer being spherical. Probably the last cells to differ-

Digitized by Illinois College of Optometry Library

entiate are the nuclei of the rods and by the 7th month the visual path is complete and capable of functioning. (That perfect vision is not, however, possible at this age can be seen by a study of the development of the macula, which at 7 months is far from perfect.)

Fig. 82 shews a section through an adult human retina for comparison. The section is, on the whole, very similar to that seen in Fig. 81, the main difference being in increased separation of the layers from each other and increased width of the inner and outer molecular layers. The inner nuclear layer also can be seen to be slightly more differentiated and shews a very definite division into:

(1) A single row of amacrine cells.

(2) Bi-polar cells interspersed with nuclei of fibres of Müller.

(3) Sparse layer of horizontal cells, much further apart than in the 7 months retina and now possessing oval nuclei arranged with their long axes parallel with the direction of the layer.

The measurements are:

a. Total thickness	0·195 mm.
b. Thickness from internal limiting membrane to amacrine cells inclusive	0·085 mm.
Ratio *b*/*a*	0·45

In the foregoing preparations very little detail can be seen of the developing *percipient elements* themselves. We have already noted that they begin to shew in the central region at about the 48 mm. stage and that their appearance marks the cessation of cell division in that area.

Fig. 83 shews the various stages of their development. In *A* we see the *cone cells* at the posterior pole in a 48 mm. human embryo. They have round or kidney-shaped nuclei, the concavity being turned towards the basement membrane, which, although it occupies the same position as the external limiting membrane in the adult, has not yet been reached by the outer processes of the Müllerian fibres. The small protoplasmic protrusions which mark the beginnings of the inner limbs of the cones can be seen, each with an exceedingly fine filament attached to the blunt apex and passing towards the pigment layer. This lies, of course, within the cavity of the primary optic vesicle and early appears to become adherent to the pigment epithelium, to which it usually remains attached if the two layers of the cup become artificially separated. This filament represents the earliest recognisable outer limb of the cone, and shews at its inception the same relations and structure as did a cilium of the basement membrane in the earlier stages.

Digitized by Illinois College of Optometry Library

In *B* we see a more advanced stage (from an 80 mm. foetus) in which the nuclei have now become spherical. The protoplasmic protrusions beyond the level of the basement membrane are longer and each one contains a pair of darkly staining particles (known as a

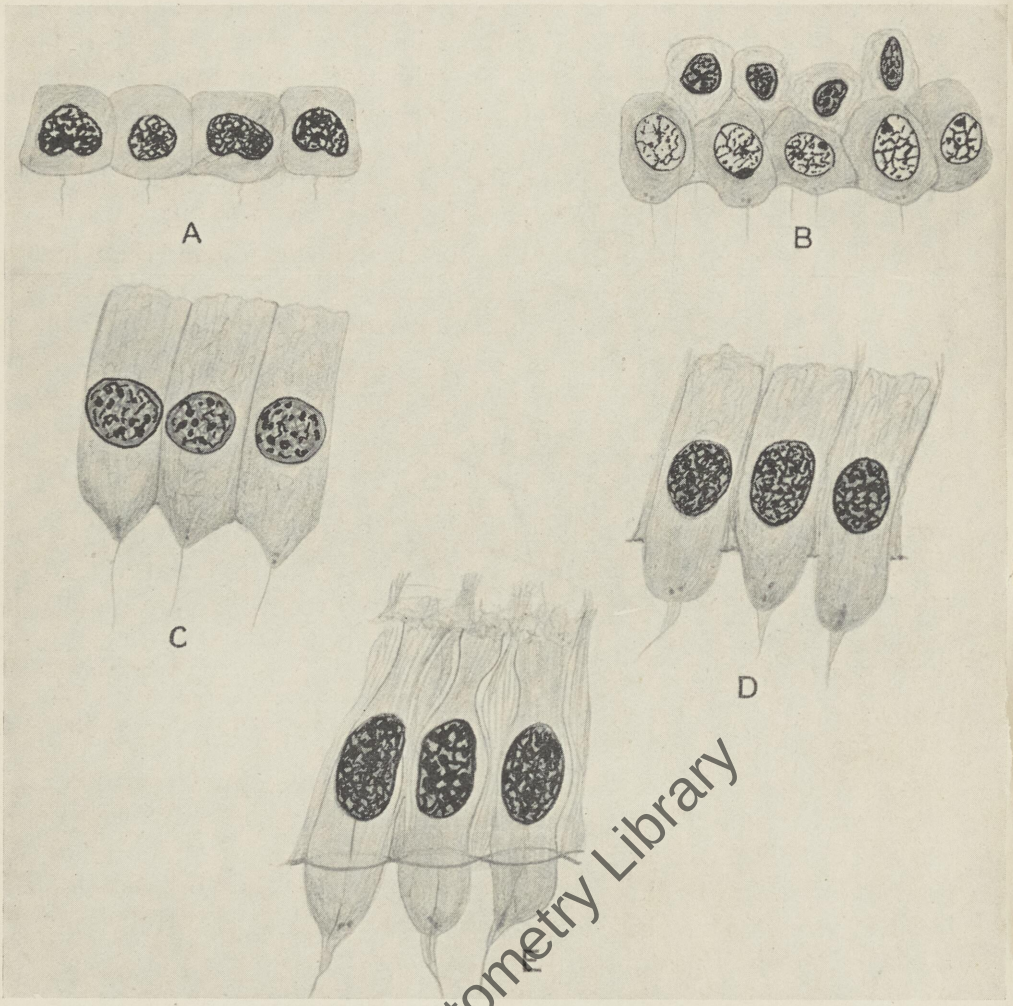


Fig. 83. Stages in the development of the retinal cones (modified from Seefelder).

diplosome) at its apex. After this the cone protrusions continue to elongate and the outer limb becomes more marked. This appears to be attached to the cell protoplasm in the region of the diplosome.

In *C* and *D* are represented further stages of this process.

E shews the young cones in a retina during the 8th month. By this time the outer processes of the Müllerian fibres (which can just

Digitized by Illinois College of Optometry Library

be distinguished in *D*) have grown as far as the basement membrane and, uniting with each other around the bases of the cones, have formed the definitive external limiting membrane, through the meshes of which the visual elements protrude. The diplosomes are still evident, and the now definitely stouter outer limb appears connected with them and with the nucleus of the cell by an extremely fine filament.

The *rods* develop in the same way but are smaller and thinner from the first. Magitot states that they can be recognised at the 7th month.

Fig. 84 shews them lying between the cones in the paracentral region.

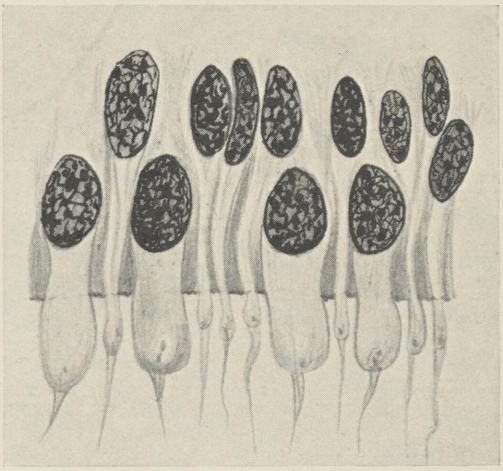


Fig. 84. Section shewing developing rods (approximately end of 7th month). (After Bach and Seefelder.)

The whole eye increases in volume after birth 3·29 times but it is probable that only in the extreme periphery of the retina is there any division of cells. Most of the increase in area is brought about by thinning of the nuclear layers (notably of the ganglion cell and bi-polar layers), the total thickness of the retina being maintained by corresponding increase of the fibre layers.

This can be seen by counting the average number of nuclei superimposed in the various layers at $5\frac{1}{2}$ and 7 months and in the adult.

Thus in the paracentral region we find:

	$5\frac{1}{2}$ months	7 months	Adult
Ganglion cells	2–3	1–2	1
Amacrine, bi-polar and horizontal cells	10	8	4–5
Nuclei of rods and cones	6–7	6–7	6–7

From an examination of roughly corresponding points in retinae at various ages it can be shewn that, after puberty at any rate, no change in retinal structure occurs, and that the retina at 80 (pathological changes excepted) presents exactly the same appearance and consists probably of identically the same cells as it did at 20. The following table shews the averages of several measurements taken in eyes of various ages. Individual variations occur, but these do not appear to be specially correlated with age.

Digitized by Illinois College of Optometry Library

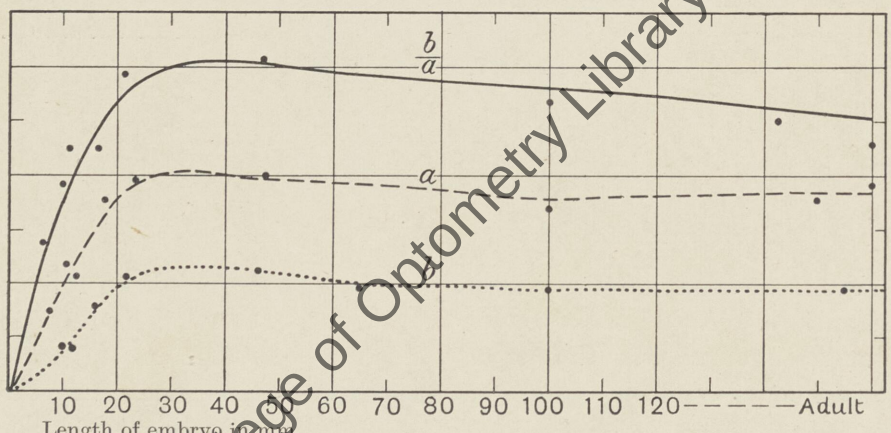
Measurements taken at the posterior pole just outside the macular region:

Number of nuclei in: Age	1. Ganglion cell layer	2. Bi-polar layer	3. Rod and cone layer	Thickness of retina measured from internal to external limiting membrane
33	2	4·5	7·5	0·225
34	2	5	7	0·2
42	1·5	5	8	0·2
46	1	4·5	7	0·25
55	1	4	7	0·2
77	1·5	6	7·5	0·225

The following table shews the measurements of the inner layer of the optic cup and of the marginal layer in the embryos described, and also the ratio between the two, from which it can be deduced that the layer of Chievitz marks the original inner level of the nuclei of the neuro-epithelium after the appearance of the marginal layer but before migration of cells into it.

Size of embryo	a = Total thickness of inner layer of optic cup mm.	b = Thickness from internal limiting membrane to layer of Chievitz or to outer edge of marginal layer according to age mm.	Ratio b/a
5 mm.	0·07	0·02	0·28
10 „	0·13	0·05	0·38
12 „	0·106	0·048	0·45
17 „	0·175	0·08	0·45
21 „	0·19	0·11	0·57
48 „	0·2	0·12	0·6
65 „	0·143	0·08	0·55
110 „	0·165	0·09	0·54
5½ months	0·148	0·072	0·48
7 „	0·175	0·08	0·45
Adult	0·2	0·085	0·425

The same result can be expressed graphically thus:



Length of embryo in mm.

- - - - a, thickness of inner layer of optic cup
. . . . . b, thickness of marginal layer
——— $\frac{b}{a}$, ratio

Fig. 85. Graph shewing growth of wall of optic cup (see text).

Digitized by Illinois College of Optometry Library

It is also apparent from these figures that practically no increase in actual thickness of the retina occurs after the 21 mm. stage, further growth being in area only[1]. This rather surprising fact is in strong contrast to the mode of growth of that other derivative of the fore-brain, the cerebral vesicle, which increases both in area and in thickness up to birth.

The development of the layers of the retina (excluding the pigment epithelium) illustrated in the foregoing pages may at this stage conveniently be summarised again thus:

Stage 1. From approx. 5 to 12 mm. (4th to 5th week).

Retina consists of a neuro-epithelium bounded on the inner side by a ciliated membrane immediately adjacent to which are cells rapidly dividing (proliferating layer), superimposed on which are other cells with nuclei arranged in several rows (primitive layer), the whole surmounted by a nucleus-free zone, the marginal layer.

Stage 2. 12–65 mm. (6th week to 3rd month).

Cells from the inner surface of the primitive layer pass into the marginal layer and form a second layer, which can be called the inner neuroblastic layer. From this are developed, by separation into layers, the ganglion cells, the amacrine cells and the fibres of Müller. The outer neuroblastic layer is present at this stage and divides later into bi-polar cells, horizontal cells and nuclei of rods and cones.

Stage 3. 65–230 mm. (3rd to 7th month).

Disappearance of space between inner and outer neuroblastic layers, with fusion of amacrine cells to bi-polar layer and separation of this last from nuclei of rods and cones.

This may be reduced to tabular form (see p. 106).

The differentiation of the layers of the retina having been dealt with, there remain two regions of the *pars optica* which still require description. These are the region of the foetal fissure and the region of the macula.

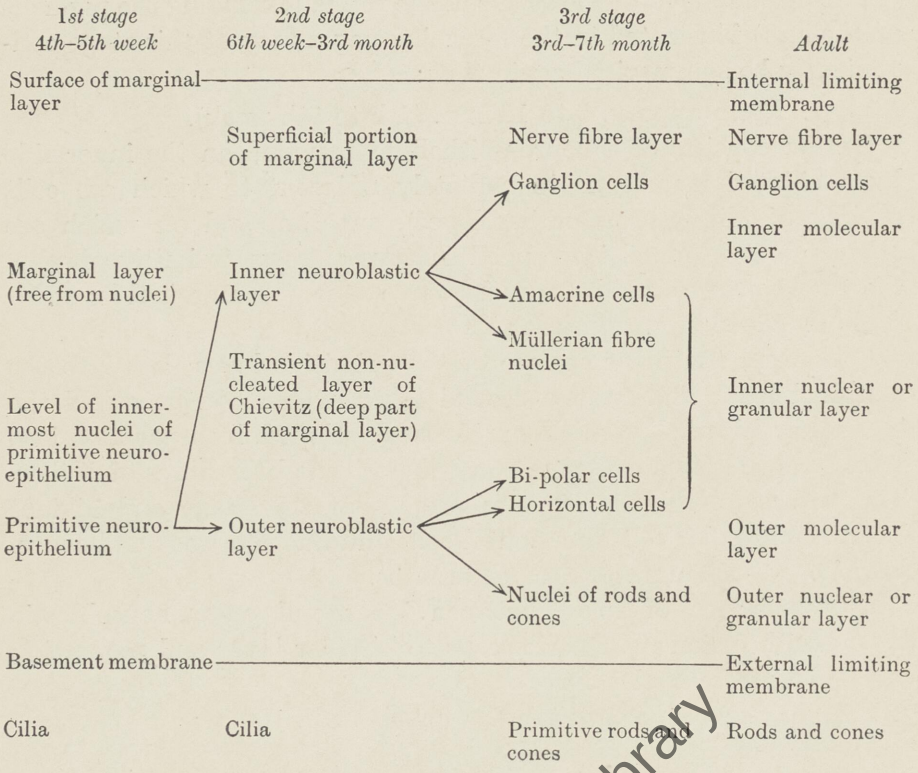
The closure of the foetal fissure. We have already seen (p. 83) that differentiation lags behind in the region of the foetal fissure. It can be considered phylogenetically the newest part of the optic

[1] The exact mode of growth of the retina is still a matter of some uncertainty. In early stages, mitotic figures, though most numerous in the proliferating layer, may be found in the inner layers as well. On the other hand, after the appearance of the rudiments of the rods and cones in any part of the retina it becomes impossible to find any mitoses whatever in that area. They are present, however, anteriorly, towards the margin of the cup, until relatively late. It is therefore generally considered that increase in size occurs during the later months solely by increment from the anterior regions. This does not, however, explain the reason for the fact that while the nuclei of the inner nuclear layer decrease in number after the third month those of the outer layer remain practically constant. Whether migration of nuclei longitudinally within a given layer occurs has not been conclusively settled, but should be considered as a possible explanatory hypothesis.

Digitized by Illinois College of Optometry Library

cup, and the process of its closure is subject to many individual modifications in various species of animals.

In man the process is relatively simple, though in order to understand it fully one must consider it in the light of other examples among the vertebrates. In the first place it must be realised that



in a large number of animals (birds, mammals, reptiles and some but apparently not all fishes) a distinct difference in growth rate is present in early stages between the inner and outer layers of the optic cup. The inner layer grows at first more rapidly than the outer and in consequence becomes thrown up into folds. This is the case in the eyes of human embryos 10–15 mm. in length. The appearance of folding is not in the early stages an artefact and has been described by Seefelder as of constant occurrence[1].

This overgrowth of the inner layer is more marked in the upper part of the eye, and in man only extends a short distance below the primitive epithelial papilla. It occurs while the cleft is still open and

[1] The folds seen later (i.e. 5th–7th month) are usually due to shrinkage of the specimen and must not be regarded as normal.

Digitized by Illinois College of Optometry Library

hence leads to slight eversion of the inner layer along the margins of the upper end of the cleft. In birds it extends lower and the portion

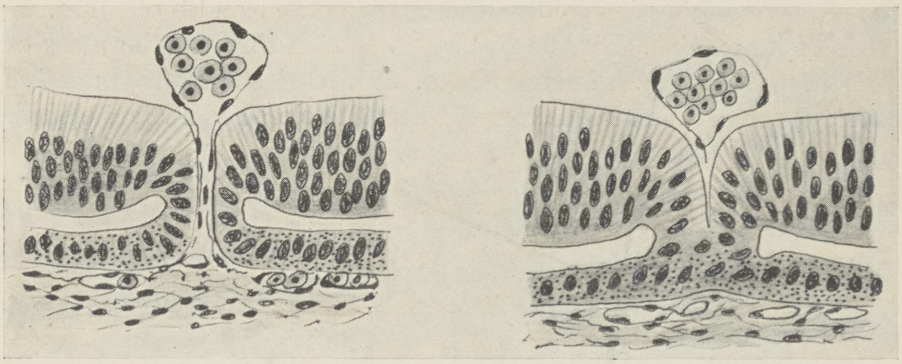


Fig. 86. Diagram shewing the process of closure of the foetal fissure in its central part.

of the cleft along which eversion occurs is much greater than in man or any of the mammals. Since pigmentation of the outer layer of the cup in most animals occurs before closure of the cleft, it follows that in the upper end of the fissure (and varying in extent with the species of animal) a non-pigmented area can be seen on the outside of the eye just below the insertion of the optic stalk. In man this area is very short. The fissure begins to close in its central part (in man) at about the 11 mm. stage and here the margins come together accurately, inner layer fusing with inner layer and outer with outer. Fig. 86 shews the process of closure in this central part. The fusion is rapid, the two layers separate and no trace whatever of the situation of the cleft remains. At the lower end the site of the fissure can be seen as a notch at the margin of the cup until the 15 mm. stage, but disappears completely after this, i.e. long before the appearance of any iris. At the upper end, where eversion has occurred, the inner layers fuse, but the everted portion of the inner layer prevents fusion of the pigmented

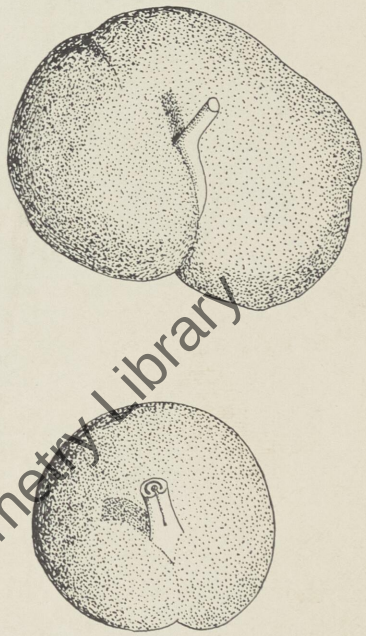


Fig. 87. The upper figure shews the posterior surface of a model of a developing avian eye, the lower one a similar view of the eye of a 15 mm. human embryo. Note in both the unpigmented area below the optic stalk.

Digitized by Illinois College of Optometry Library

layers and a small pale area is left below the optic stalk. Fig. 87 shews this area in a human embryo of 15 mm. and in a bird. In the bird the area is longer, persists and undergoes further differentiation: in man the cells composing it rapidly become pigmented and by 20 mm. no trace of it remains. Fig. 88 *B* shews a section through the mass of cells in the 15 mm. human embryo. Fig. 88 *A* shews (in the same embryo) the eversion in the region where the cleft has not yet closed.

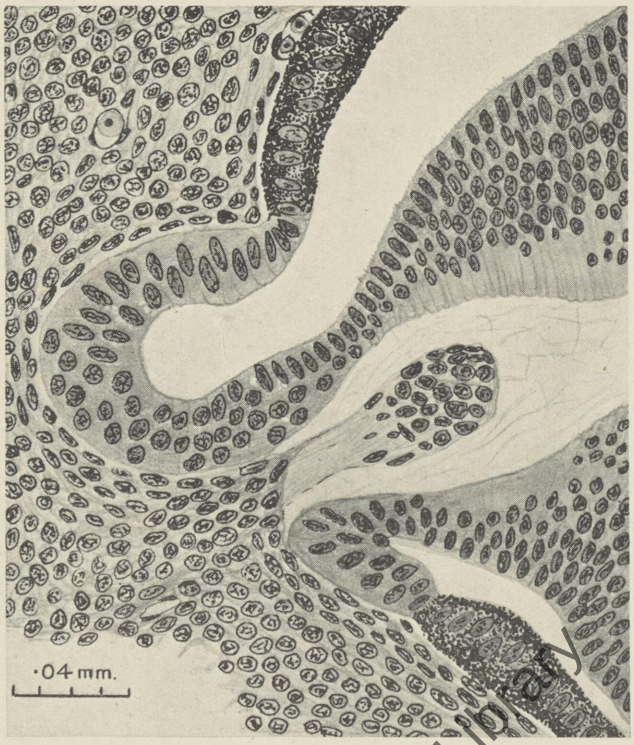


Fig. 88 *A*. Section through the posterior pole of the eye of a 15 mm. human embryo, passing through the open portion of the foetal fissure. The eversion of the non-pigmented inner wall of the cup is seen. The hyaloid artery is entering the cup between the lips of the fissure.

The extreme upper end of the cleft in man never closes, but remains as the passage of entry of the arteria centralis retinae in the centre of the disc. The inner aspect of the upper end of the cleft in man also requires description. It has been noted that before growth of nerve fibres from ganglion cells around this upper end, the site of the optic disc can be recognised as the "primitive epithelial papilla." The cells forming the papilla are merely the cells of that part of the inner wall of the optic cup which surrounds the upper end of the fissure. Before the appearance of nerve fibres they are in direct

Digitized by Illinois College of Optometry Library

continuity with the cells of the rest of the inner wall. When the first nerve fibres appear these grow towards the epithelial papilla and pass through its substance into the inner layer of the optic stalk. Most of the cells of the primitive epithelial papilla disappear as the nerve fibres increase in number, but a few of them remain in the centre of the nervous papilla, separated by the nerve fibres from their fellows in the retinal layers around the papilla.

Fig. 89 shews in a schematic manner how this occurs, and how these sequestrated cells come to form a little cone-shaped mass of

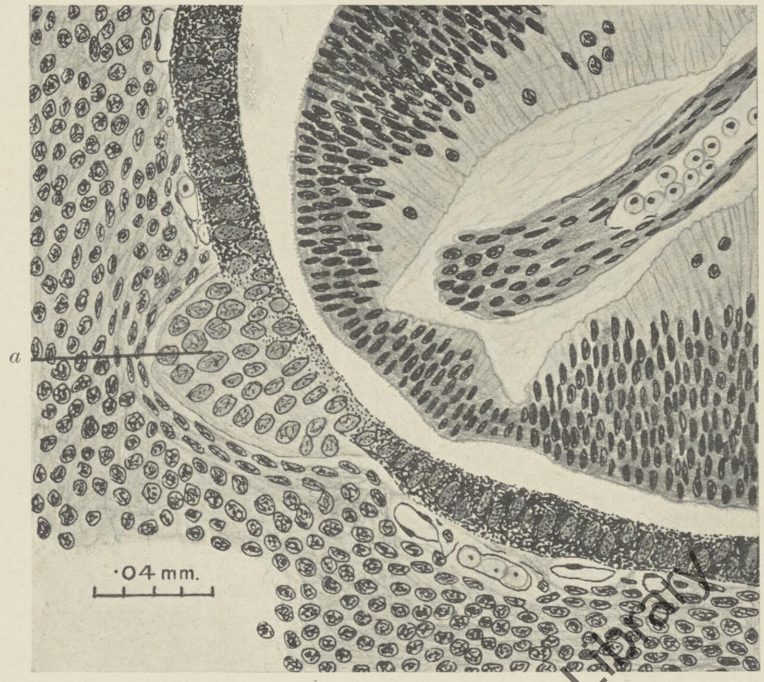


Fig. 88 *B*. Section through the posterior pole of the eye of a 15 mm. human embryo. The section passes through the upper end of the fused portion of the foetal fissure. *a*, mass of unpigmented cells formed by fusion of the everted portions of the inner layer of the cup.

nuclei in the centre of the disc. This cone is known as "*Bergmeister's papilla.*"

It has been described in a large number of mammals but reaches its highest development in birds, in which the cells forming it proliferate and constitute the rudiment of the pecten. This organ forms from them and added vascular mesoderm in all those Sauropsidans which possess it. Fig. 234 shews Bergmeister's papilla in the chick.

In man the size of this papilla is rather variable. It is well seen in Fig. 203 *b*, which shews the optic disc of a 32 mm. human embryo. The cells forming the papilla are glial in nature and proliferate during

Digitized by Illinois College of Optometry Library

the 5th month to form the glial sheath of the hyaloid artery (Fig. 203 *a*). This sheath and the papilla of Bergmeister atrophy with the hyaloid before birth. The exact amount of atrophy determines the depth of the "physiological cup" in the centre of the disc, this being the depression left by the absorption of the cone of cells.

The development of the macula lutea and the fovea centralis. Fig. 90 shews the well-known arrangement of the nerve fibres on the inner surface of the adult retina. It will be seen that those on the temporal side (the macular region) diverge from a line passing horizontally outwards and run upwards and downwards from this

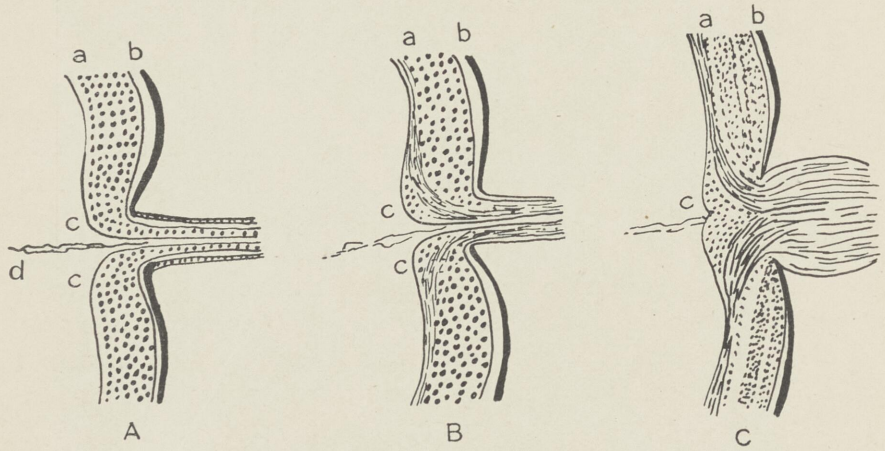


Fig. 89. Scheme shewing the development of Bergmeister's papilla. *A*, Horizontal section through the upper end of the fissure before the appearance of nerve fibres. *a*, inner wall of cup and stalk; *b*, outer wall of cup and stalk; *c*, primitive epithelial papilla; *d*, hyaloid artery. *B*, Similar section just after appearance of nerve fibres. *c*, cells of epithelial papilla cut off by issuing nerve fibres. *C*, Similar section through the newly formed nervous papilla. *c*, Bergmeister's papilla in centre of nervous papilla.

to curve round and converge on the central third of the temporal side of the disc as the papillo-macular bundle. This arrangement is at first sight very suggestive of a horizontal cleft running out from the disc, and various attempts have been made in the past to account for it on developmental grounds. It has been suggested that the apparent line of separation of the nerve fibres represented the line of the foetal fissure and that the macula lutea was developed from the walls of the cleft. If this is the case, then rotation through at least 80° must have taken place to bring the fissure, which is at first on the under side of the cup, round to the position of the macula (see p. 44). There is, however, very little positive evidence that any rotation occurs at all, and none whatever to shew that the macula has any connection with the fissure. Indeed we have already seen

Digitized by Illinois College of Optometry Library

that the region bounding the cleft represents the most recent portion of the optic cup and that differentiation lags perceptibly behind along its margin. Also we have seen that the region of the posterior pole above and to the temporal side of the disc may be looked on as the phylogenetically oldest portion and that differentiation here is, quite early in embryonic life, more advanced than elsewhere in the retina. Since the macula lutea represents the highest stage of development reached by any part of the human eye, it appears on *a priori* grounds more likely that it should develop as a final stage in the region which is from the beginning more specialised than the

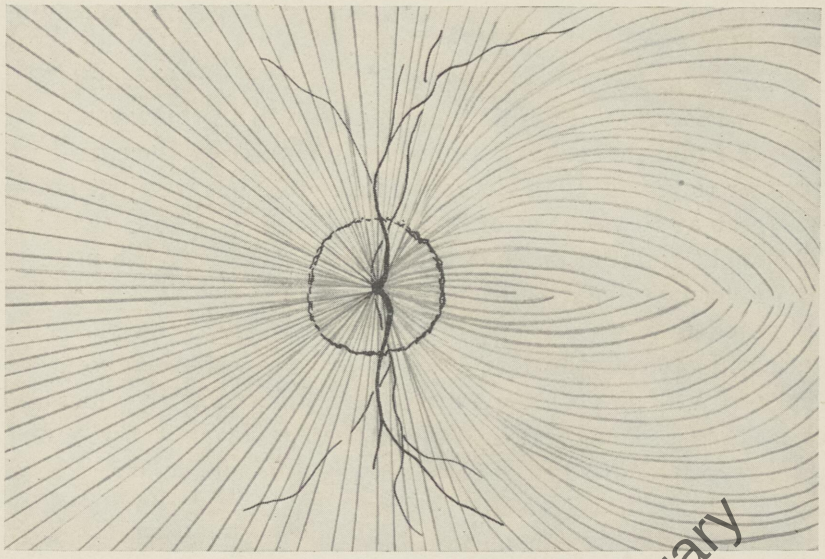


Fig. 90. Diagram shewing the arrangement of nerve fibres on the inner surface of the adult retina. The macular region is on the right.

rest. This is now known to be the case and since the work of Chievitz on the macula in human foetuses the older views connecting the macula with the cleft have been completely discarded. The arrangement of the nerve fibres is probably merely a correlate of the order in which they appear, those near the disc on the temporal side forming first and the others, further out, sweeping round them above and below to reach the disc by the most open route.

The region of the future macula lutea shews as early as the 3rd month some indication of its situation. At this stage we have seen that the position of the line of separation between the inner and outer neuroblastic layers can be recognised over the whole retina. In the equatorial and peripheral regions there is no longer an actual

Digitized by Illinois College of Optometry Library

fibre layer as there is in earlier stages (layer of Chievitz), the line being merely marked by a difference in shape of the nuclei on either side of it. In the central region at this stage, however, the layer of Chievitz retains a definite thickness and is free from nuclei. At the 3rd month the macular region begins to lag slightly behind the rest of the retina. This slight retardation of development is quite apparent from the 3rd till the 8th month, after which development proceeds along highly characteristic and specialised lines; the specialisation of the rest of the retina is almost complete by the 9th month and development practically ceases, while in the central region it continues apace until at least 16 weeks after birth, the slight initial retardation being thus correlated with a longer growth period and a more highly specialised final condition.

In the central region the layer of Chievitz persists and becomes gradually wider, attaining its maximum width in the fovea centralis at the 8th month. It persists in the immediate paracentral region for longer than it does in the fovea itself and can still just be recognised there at 10 weeks after birth.

The slight retardation of development marked by the persistence of the layer of Chievitz affects the other retinal layers as well. We have noted that, as division in the proliferating layer slows down, increase in area of the retina takes place by thinning out of the nuclei and widening of the fibre layers. The thinning does not at first involve the macular region, so that at 6 months the nuclear layers, especially the ganglion cell layer, are thicker here than elsewhere. This makes the macula appear as a slight heaping up (Fig. 91) and not as a depression at this stage. The ganglion cell layer is 7–9 cells deep, as against 4 in the paracentral region. The amacrine cells are 2–3 deep and the bi-polars 3–4. Elsewhere the amacrines are reduced to a single row and lie in direct contact with the bi-polars (Seefelder).

The first sign of a depression at the fovea can be recognised at 7 months. At this stage (Fig. 91) the ganglion cell layer is beginning to thin in the fovea and is only now 4 cells thick at the bottom of the depression. The layer of Chievitz is slightly wider than it was at 6 months, and also the external molecular layer is much better marked than before. The percipient elements themselves, however, are not nearly so advanced at the macula as they are elsewhere, resembling rather those seen in Fig. 83 *C* than in 83 *E*.

The slight depression seen at the fovea at 7 months deepens as the ganglion cell layer thins, so that at 8 months it forms a broad saucer-shaped hollow. The ganglion cells at its deepest part are

Digitized by Illinois College of Optometry Library

now only two deep, though at the periphery of the macula there are still 4–5 rows of them. The layer of Chievitz is wider, especially just at the edge of the central fovea. The bi-polar layer shews signs of

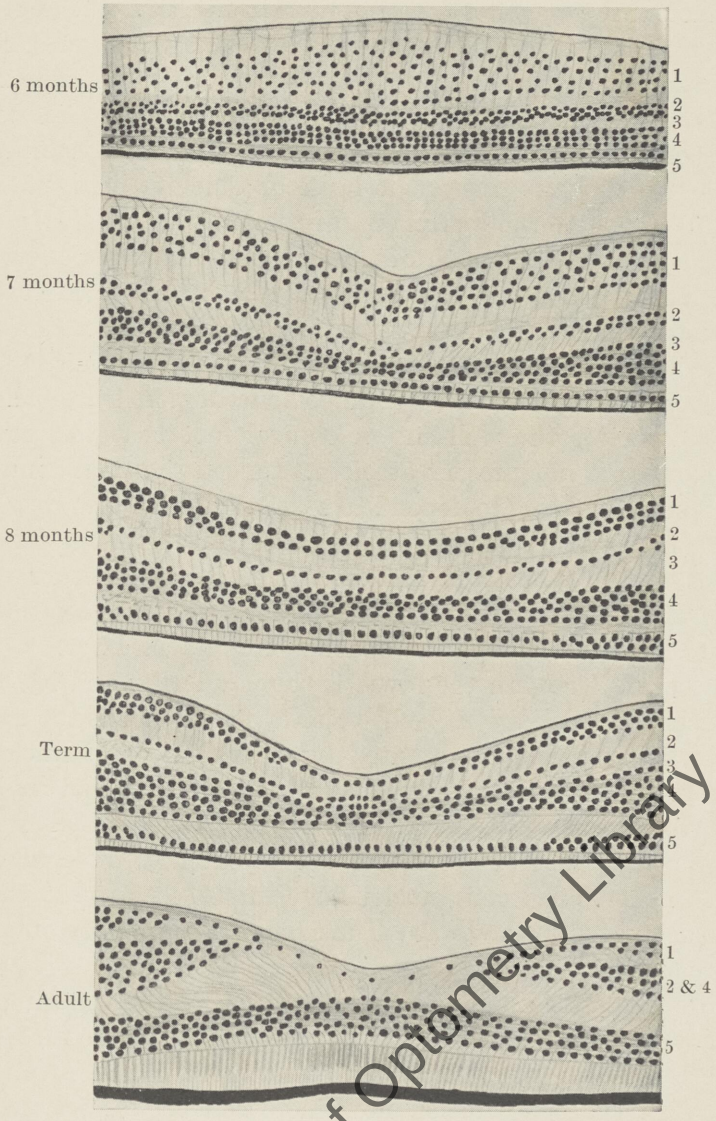


Fig. 91. Five schematic representations of the macular region at 6 months, 7 months, 8 months, term and in the adult respectively. 1, ganglion cell layer; 2, amacrine cells; 3, layer of Chievitz; 4, bi-polar nuclei; 5, nuclei of cones.

slight thinning by this stage, but all the nuclear layers are still well represented all over the macula and fovea. Slight individual variations in the shape and size of the fovea can be recognised from now

Digitized by Illinois College of Optometry Library

onwards, in the same way that the shape of the macular reflex can be seen to vary remarkably in the adult, especially if a series of presumably normal subjects are examined by the ophthalmoscope in red-free light.

The macular region at birth can be seen in Fig. 91. The depression in the centre is deeper and the thinning of the ganglion cell layer more marked, it being now reduced in the fovea to a single row of nuclei. The bi-polar layer is also thinner here, being reduced to 3–4 tiers of nuclei only, this including the layer of amacrine cells which has fused with it here, the layer of Chievitz being now only perceptible towards the periphery of the fovea. There is also a marked increase in the width of the external molecular layer. The cone nuclei form a single row in the fovea, but have increased to two and sometimes three rows at the periphery of the macula. The cones themselves do not yet appear any longer than their fellows in the paracentral regions. This arrangement demonstrates the anatomical reason for the well-known clinical fact that the power of central fixation is not present at birth. Indeed the final completion of development appears to depend to a certain extent on the stimulus of light, since it can be shewn that in cases in which the formation of images at the macula is hindered (e.g. by cataract or corneal scarring) at or soon after birth, the power of central fixation may never develop, even though the opacity be removed later.

At 8 weeks after birth the fovea is slightly larger and its bottom more flattened. In addition the bi-polar layer, as well as the ganglion cell layer, is now only represented by a single row of nuclei. The nerve fibre layer is practically absent and the internal molecular layer narrower than elsewhere. The layer of Chievitz can still be seen at the periphery of the macula. The external molecular layer is much thicker. The cone nuclei have increased so that they are now two deep even in the fovea. The cones are more fully developed, and more slender.

By 16 weeks after birth we can recognise that the thinning of the ganglion cell and bi-polar layers has progressed even further and that the few nuclei which now represent them in the fovea are in contact with the cone nuclei, now increased to 3 rows deep. In addition, the cones in the fovea have increased in length, so that a curve, concave outwards, can be recognised in the external limiting membrane; this corresponds in position with the depression of the fovea on the inner surface of the retina and is hence sometimes known as the *fovea externa*. The layer of Chievitz can only just be recognised here and there. The macula is now practically complete.

Digitized by Illinois College of Optometry Library

Fig. 91 shews an adult macula for comparison. It will be seen that the bi-polar layer has completely disappeared and the ganglion cell layer almost completely in the fovea. The cone nuclei have increased in number still further (4–5 rows) and the individual cones have become longer and thinner, with the result that the fovea externa is more marked. There is no trace whatever of the layer of Chievitz. The external molecular layer is thicker except in the centre of the fovea.

From these foregoing stages one may summarise the development of the central region of the retina by stating that it can be divided into 3 periods as follows:

1. *First period*, from the time of invagination of the optic cup till the 3rd month (65 mm.). Throughout this period the central region is at any age the most differentiated portion of the retina. The division into two neuroblastic layers occurs first at the posterior pole, as also does the separation of the other layers from these.

2. *Second period*, from the 3rd to the 8th month (65 to 250 mm.). This is characterised by a retardation of differentiation in the macular region. The nuclear layers do not thin so markedly, nor does the layer of Chievitz disappear so rapidly as in other parts of the retina. The cones also remain more rudimentary although they were first appreciable here.

3. *Third period*, from 8th month of intra-uterine life to 4th month after birth. This is the period of macular differentiation proper, the preceding two stages being merely preparatory. During this period the nuclear and bi-polar layers thin, the cone nuclei increase in number, the cones themselves become highly specialised and the fovea externa develops in consequence.

B. Pars Ciliaris Retinae

The *pars ciliaris retinae* must now be considered[1]. There is no trace of iris or ciliary body before closure of the fissure. The edge of the optic cup only reaches as far as the equator of the lens (Fig. 43) and the structures which appear subsequently in front of this are formed by forward growth of the margin of the cup. This growth begins just before the 48 mm. stage. In Figs. 52 and 74 can be seen the anterior part of the eye of a 48 mm. embryo in which an extension forwards of a double layer of epithelium (separated widely by the remains of the cavity of the primary optic vesicle) is taking place

[1] The iris and ciliary body consist of both mesodermal and ectodermal elements. Only the ectodermal components will be dealt with in this section, as that alone can be considered part of the retina.

Digitized by Illinois College of Optometry Library

from the margin of the optic cup. The outer layer (outer wall of optic cup) is pigmented, but this condition does not extend quite to the margin of the cup, the inner layer (or wall of cup) appearing of more exuberant growth so that it turns over the edge, somewhat in the way in which it was seen to do in the upper part of the fissure (Fig. 88 *A*). There are a few folds in the inner layer of the ciliary processes. The folding does not at present involve the outer layer at all. The next stage (65 mm.) (Figs. 29 and 34) shews how the folding is beginning to involve the outer layer also and how the pigmentation is spreading up to the growing margin. The cells of the outer layer at this margin are also shewing the first signs of differentiation. Adhesion is beginning between inner and outer layers of the optic cup here, except just at the growing tip, where the cavity of the primary optic vesicle is still patent. The space thus left is usually referred to as the "marginal sinus."

At this stage the extreme tip can be said to represent the pupillary border of the iris, and the folded part the future ciliary processes, while the regions of the pars plana and the ora serrata cannot be recognised at all, although, of course, an area of gradual transition from more complex to less complex retinal structure can be seen at the base of the folds.

From this stage onwards the growing tip extends forwards, leaving the folded portion behind. This becomes more folded still, both layers participating, and in its turn extends farther forwards, leaving behind it as it does so a smooth region composed of two epithelial layers only, the *pars plana*. This is a slow process, and even by the 5th month the *pars plana* is hardly visible. By the 7th month the *ora serrata* lies on a level with the middle of the ciliary muscle, by the 8th month with its posterior third, by the 9th month with its posterior border and at birth behind it. These measurements apply to the temporal half of the eye, the pars plana being slightly narrower than this in the nasal half. At birth and even in the adult, individual variations are common and mostly take the form of toothed processes of the pars optica which extend here and there up to the ciliary processes. They are said to be more common in hypermetropic and malformed eyes.

Very soon after their appearance (i.e. during the 3rd month) the little folds in the edge of the optic cup come to involve both the inner and the outer layer and to arrange themselves in a definite radial manner all round the margin, extending not quite to the growing edge. They number from their inception 70–75 and each one differentiates into a single ciliary process. They are formed of

Digitized by Illinois College of Optometry Library

two layers of neuro-epithelium derived respectively from the inner and outer layers of the cup. Each layer is formed of a single row of short columnar cells, the outer layer being densely pigmented from the first. The inner surface of the inner layer is not covered by any *membrana limitans interna*, since there are no fibres of Müller in this region. The surface is irregular, and cone-shaped processes and fine filaments are attached to the cells, so that they resemble the cells

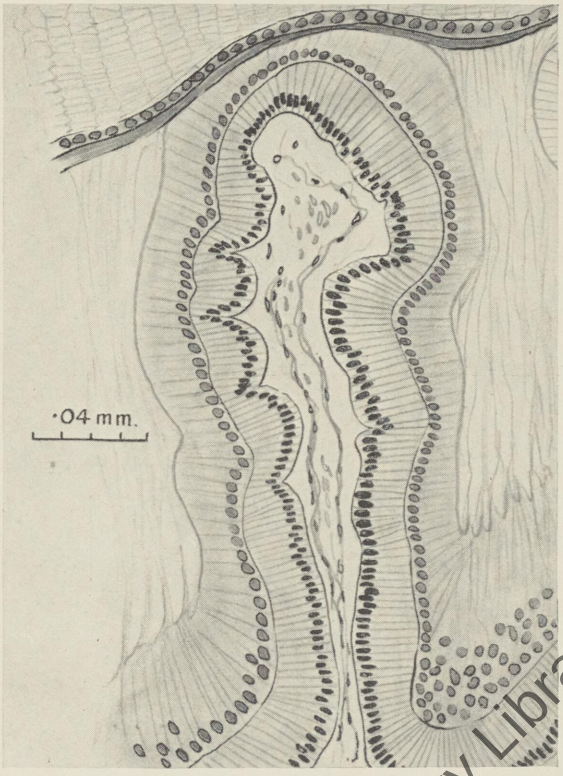


Fig. 92. Section through a ciliary process (bleached) from a 110 mm. foetus. The epithelium of the lens is seen in contact with the apex of the process (above).

of the primitive retina of the 4 and 5 mm. stages. (This will be referred to in greater detail when the vitreous is dealt with.) The cells on the summits of the processes very soon shew signs of a definite smooth surface, but those in the valleys retain their primitive irregular edge for some time longer and indeed never fully differentiate.

Each epithelial ciliary process has a mesodermal core containing a blood vessel derived from the choroidal net which covers the outside of the optic cup. The valleys between the processes increase in depth

Digitized by Illinois College of Optometry Library

and the summits come in contact with the equator of the lens at 4 months (110 mm.).

Fig. 92 shews a single ciliary process (from an equatorial section of the eye of a 110 mm. foetus) which has been bleached to remove

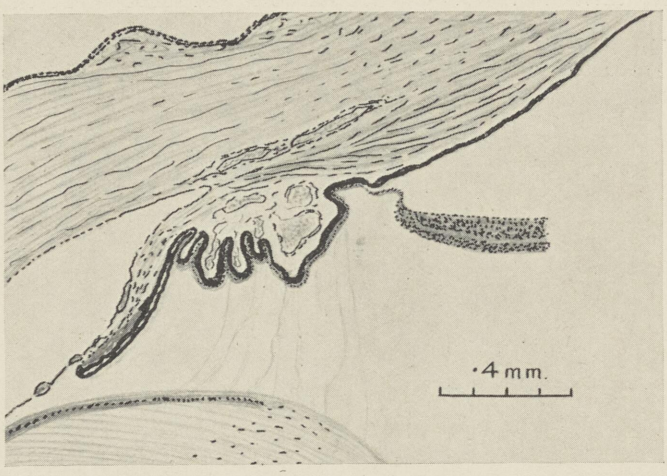


Fig. 93. Section through the ciliary region and iris of a 5½ months foetus (circ. 170 mm.).

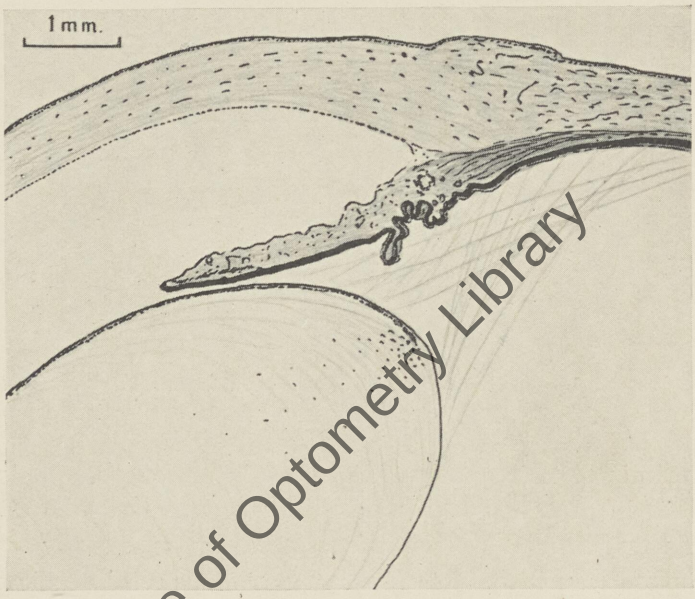


Fig. 94. Section through the ciliary body and iris of an adult human eye.

the pigment and to allow the cells of the outer layer to be seen. Both layers of epithelium are columnar and in both the nuclei lie at the outer ends of the cells. The nuclei of the pigment layer stain

Digitized by Illinois College of Optometry Library

more darkly than the others. The inner surface of the inner layer is quite smooth and sharply defined on the summit of the process, but in the valley the cells are irregular, longer and shew innumerable projecting fibres, which fill the space between the adjacent processes, and are attached to the lens capsule.

The outer layer covering the process is becoming thrown up into little folds and in some places these appear to involve the inner layer also. This folding of the outer layer is the first recognisable indication of the development of the structures known as the **glands of Collins,** which can be found in the adult (in bleached specimens), and the function of which is believed to be the secretion of the aqueous humor.

The ciliary region does not alter much after the 4th month except that the tips of the processes become further removed from the lens and the *pars plana* appears. The epithelium remains as a simple double layer throughout life, the inner layer never becoming pigmented. Fig. 93 shews a low power view of the ciliary region at $5\frac{1}{2}$ months and Fig. 94 the same part in the adult.

C. Pars Iridica Retinae

The *pars iridica retinae* develops by the forward growth of the margin of the optic cup in front of the ciliary region. It includes, considered from a developmental point of view, the double layer of pigmented epithelium which covers the posterior surface of the adult iris, and also the derivatives of this, the sphincter and dilatator muscles of the pupil. The adult iris consists of these structures *plus* a stratum of mesoderm on its anterior surface, the *iris stroma*. This stroma and its relations in the embryo will be more fully described in Section VI, but for the complete comprehension of the development of the margin of the optic cup it is necessary to realise the following two points.

In the *first* place it must be clearly understood that the opening or pupillary rim of the optic cup ceases to be in direct contact with surface ectoderm at the time of the appearance of the lens vesicle. As this vesicle separates from the surface ectoderm and sinks into the optic cup, the mesoderm in which this latter is embedded grows rapidly forwards around its anterior aspect and comes to form a layer lying between the optic cup and the lens vesicle on the one hand, and the surface ectoderm on the other. This layer of mesoderm completely closes in the anterior opening of the optic cup or pupil, as it may presumably be styled, even although the iris is not yet present.

Digitized by Illinois College of Optometry Library

The *second* point which must be made at this stage is that, although various important modifications occur in this layer of mesoderm, its relation to the pupil is not altered until late in foetal life (when a portion of its central part disappears) with the result that when, at the 3rd month, the margin of the optic cup begins to grow forward to form the epithelial layers of the iris, it has mesoderm already in contact with its anterior surface and simply grows forwards deep to and in contact with this mesoderm, which is destined to form the definitive iris stroma. Thus the iris may be divided embryologically into a mesodermal and an ectodermal portion and of these the

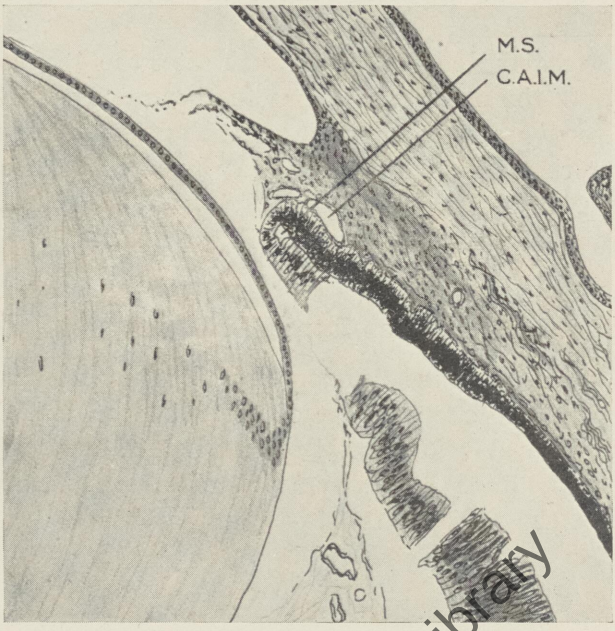


Fig. 95. Section through the margin of the optic cup of a 65 mm. human embryo. *M.S.*, marginal sinus; *C.A.I.M.*, circulus arteriosus iridis major.

mesodermal portion appears first and is already *in sitû* before the ectodermal portion begins to develop.

We are now concerned with the growth of the *ectodermal* lining portion. The first signs of this are apparent at the end of the 3rd month, when the margin of the optic cup begins to give indications of active differentiation and the ciliary folds are just commencing. It is obvious that the margin of the optic cup, as it grows forward, must consist of two layers continuous with the inner and outer walls of the cup respectively. Since, however, the two layers are extending in a curve around a spherical surface, when they reach the front surface of the lens they can be described as anterior and pos-

Digitized by Illinois College of Optometry Library

terior instead of inner and outer. The anterior layer of the iris epithelium is obviously directly continuous with the outer wall of the optic cup further back (i.e. pigment layer of retina), and the posterior layer of the iris with the inner wall of the optic cup.

Differentiation of the anterior and posterior layers of the ectodermal iris continues *pari passû* with the forward growth of the whole margin of the optic cup. At the 3rd month both layers of the cup at the growing edge are composed of columnar cells arranged in a single row. Those of the anterior layer are pigmented, but not those

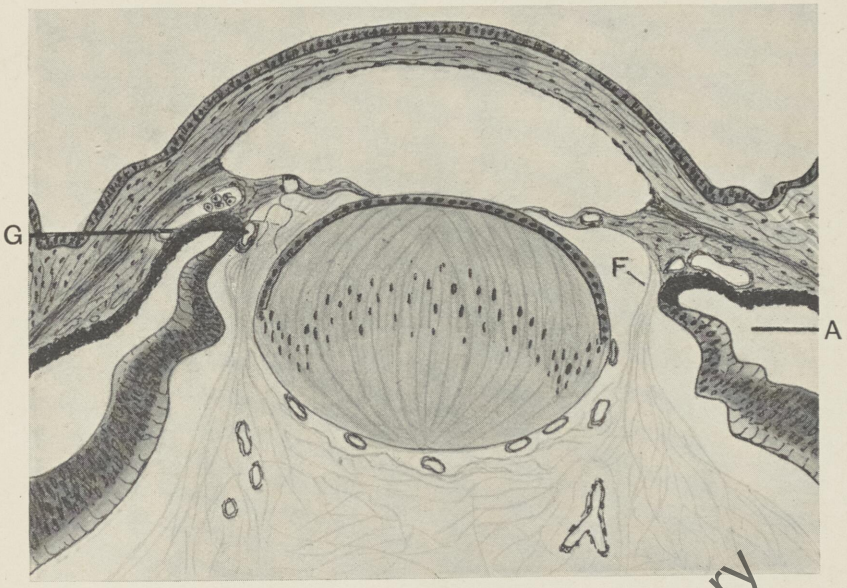


Fig. 96. Section through the anterior part of the eye of a 48 mm. human embryo. *A*, remains of cavity of primary optic vesicle; *F*, "faisceau isthmique" of vitreous (see p. 179); *G*, remains of capsulo-pupillary vessel (see p. 205 et seq.).

of the posterior layer at this stage. At the extreme edge, just where the anterior layer turns over to become the posterior layer, the cells are cubical for a short distance and have only a few grains of pigment in them. The remains of the space between the two layers of the optic cup can be seen as a little circular channel in cross-section (Fig. 95) and is known as the *marginal sinus*. This appearance of a narrow tubular channel is due to the fact that elsewhere at this stage the layers of the optic cup are commencing to come into apposition. The sinus cannot be seen before this stage since in the younger eyes the two layers of the optic cup are everywhere separated by a space, which in some preparations appears wide, in others narrow.

Fig. 96 shows the growing edge in a 48 mm. human embryo and

Digitized by Illinois College of Optometry Library

makes this difference clear. Fig. 97 shews a high power view of the margin of the cup in the 65 mm. embryo shewn in Figs. 34 and 95. It will be seen that differentiation is beginning in the *anterior layer*. The cells of this layer are rather more columnar near the margin of the cup than elsewhere and the pigment is aggregated in the deeper parts of the cells. This tendency for the outer ends of the cells at the margin to appear clearer than the inner ends can first be recognised about 25 mm. but becomes rather more marked in the 3rd month. The marginal sinus is at this stage quite definite, but very small.

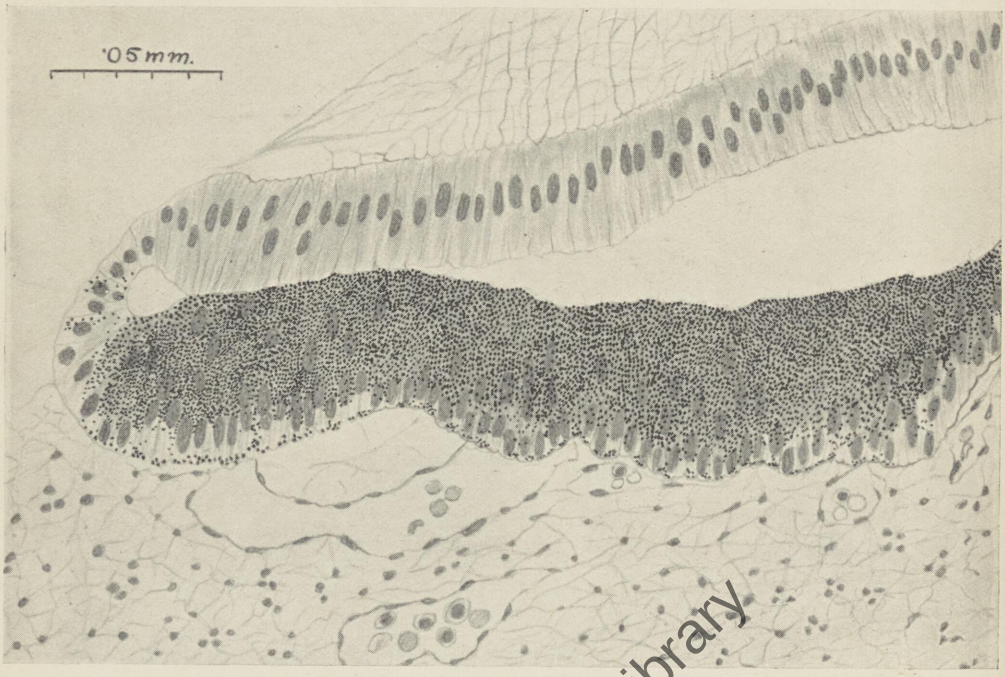


Fig. 97. Section through the growing margin of the optic cup of a 65 mm. human embryo. The inner layer is unpigmented and is seen in the upper part of the drawing. The outer (pigmented) layer is below.

The marginal sinus increases as the iris grows, so that, at five months, i.e. at the time of most active growth and differentiation of the edge of the cup, it is very large. After this it gets smaller and has disappeared by the 7th month when growth is slowing down again. The persistence of this portion of the cavity of the primary optic vesicle for so long appears to be correlated with the late differentiation of the iris and is probably the expression of the rapid change of shape, size and position of the growing edge whereby cohesion between the layers is rendered more difficult here than in the more firmly established retinal area.

Digitized by Illinois College of Optometry Library

The posterior layer of the ectodermal iris does not undergo any elaborate differentiation. The cells, which, as we have seen, are columnar at the 3rd month, become gradually flatter and thicker so that by five months they are definitely cubical in form. They become gradually pigmented; the pigmentation extends from the anterior layer around the marginal sinus and thence backwards along the posterior layer from the pupil border towards the ciliary region. The deposit of pigment is slow and occupies the period from the end of the

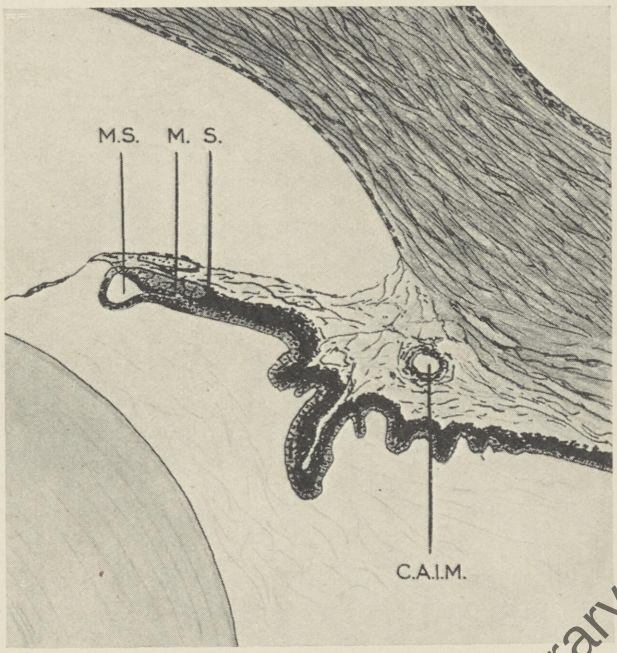


Fig. 98. Section through the iris and ciliary body of a human foetus of 5 months (150 mm. approx.). *M.S.*, marginal sinus; *M.*, sphincter pupillae; *S.*, Michel's pigment spur; *C.A.I.M.*, circulus arteriosus iridis major.

third month to the *seventh*, by which time it has reached the base of the ciliary processes at the iris root: it spreads no further even in adult life.

Figs. 98 and 99 shew this pigmentation in progress in a foetus of 5 months. It will be seen that the cells are involved halfway along the posterior surface of the iris only.

The anterior layer of the ectodermal iris undergoes a much more elaborate and curious differentiation. This includes the development from it of two muscles, the *sphincter* and the *dilatator pupillae*. These two muscles therefore form an important exception to the general rule that muscle fibres, both striped and unstriped, are developed from mesoderm. The *arrectores pilorum* of the skin form the only

Digitized by Illinois College of Optometry Library

other known exception in man, but they are developed from surface ectoderm, while the pupil muscles come from the neural ectoderm of the optic cup. This mode of development marks them out as being extremely primitive in type, and accords well with the known fact that in many of the lower animals (especially amphibians), and to a lesser extent in man also (Hertel), the sphincter pupillae possesses the power of contracting under the direct stimulus of light, when all nerve paths have been put out of action (either by experiment or pathological change). This leads us on to draw a rather fantastic

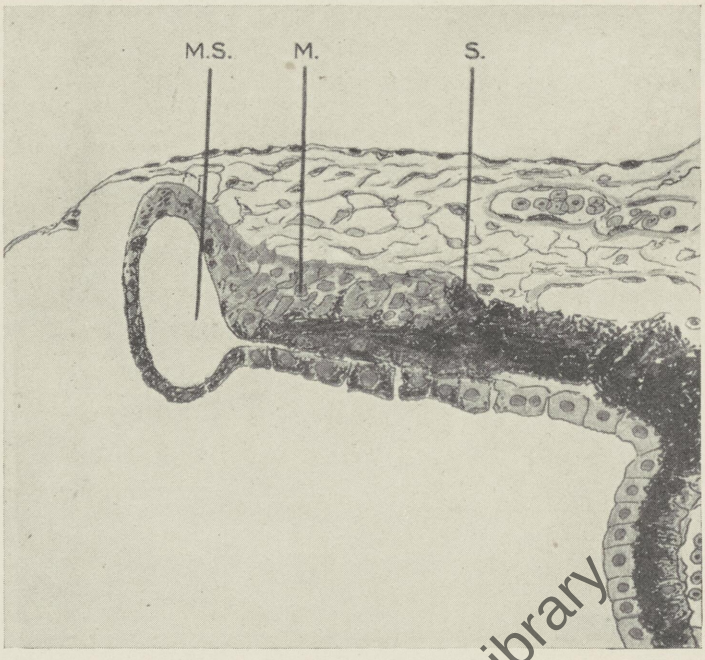


Fig. 99. Higher power view of the iris alone from the same specimen as Fig. 98. *M.S.*, marginal sinus; *M.*, sphincter pupillae; *S.*, Michel's spur.

analogy between the iris muscles and the contractile arrangements of the primitive two-layered invertebrates, which afford examples of the lowest grade of phylogenetic muscle development. In such an animal as Hydra there are present in the two-layered body-wall certain specialised cells which reach from outer to inner surface. The outer end of such a cell is armed with a sensitive projecting cilium and acts as the receptor of a tactile stimulus, while the inner end of the same cell shews cross striations and is contractile. This inner part shortens when the cilium is stimulated and so draws the body away from the stimulus. Such a cell can be looked on as a complete neuro-muscular complex or reflex arc in itself, and cannot be said

Digitized by Illinois College of Optometry Library

to be either mesodermal or ectodermal, muscular or nervous in nature. As phylogenetic development proceeds, the three functions which the cell subserves (reception, conduction and contraction) become relegated to three separate cells and a true reflex arc is established, the first two links in the chain being usually developed from surface ectoderm and the third from a new germinal layer, mesoderm, which has arisen at the same time.

Fig. 100 makes this clear. The muscle fibres of the iris can be looked on as representing a combination of the two conditions, the specialised and the primitive, since although they possess a nerve supply and are therefore relegated, generally speaking, to the position of one link only in the reflex chain, yet, under suitable conditions, they are still capable of functioning by themselves both as receptor and contractor without the intervention of any nerve paths at all.

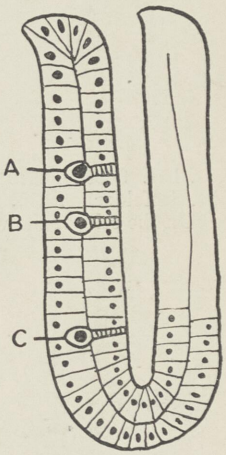


Fig. 100. Diagrammatic representation of the body of a two-layered invertebrate (Coelenterate). The cells *A*, *B* and *C* are specialised and possess a projecting cilium, a cell body and a contractile process directed inwards. These pass through the outer layer of cells (ectoderm) and reach the inner (entoderm) which lines the alimentary cavity.

The mode of development of the **sphincter of the pupil** in man is as follows. Its earliest appearance is during the 4th month when, by means of special staining (Held's method—Seefelder), traces of fibrillae can be seen in the protoplasm of the anterior layer at the extreme edge of the iris. The cells in which it appears are those small cubical ones noted as surrounding the marginal sinus at 65 mm.

Fig. 101 shews this stage. As yet there is no trace of the dilatator pupillae. The growth of both layers forwards continues and soon, probably through slightly more rapid growth of the posterior layer, the little mass of specialising cells comes to lie in the anterior wall of the marginal sinus, not at its extreme margin as before. Fig. 102 makes this clear. It continues to occupy this position and increases in width as the iris grows. The cells which are going to form the sphincter now become sharply marked off from the underlying cells from which they were derived, since these latter contain pigment and the muscle cells do not. The sphincter is slightly sunk into the substance of the pigmented part and its peripheral limit is marked by a little ridge of pigment which partially overlaps it. In transverse section this looks like a projecting process and is known as *Michel's spur*. Other irregular spur-like projections of pigmented cells into

Digitized by Illinois College of Optometry Library

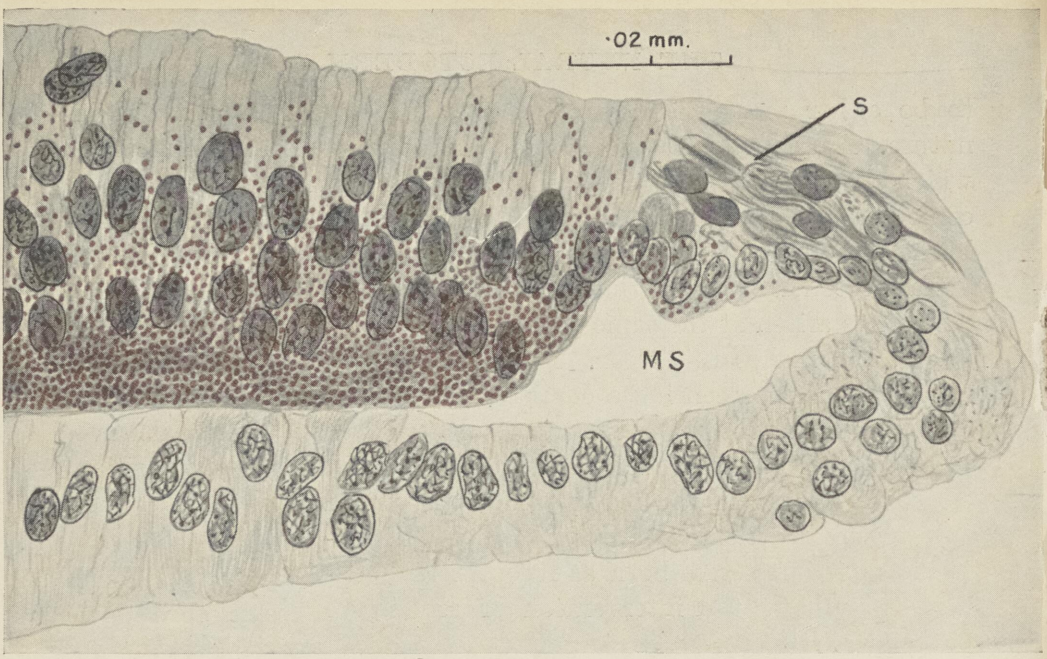


Fig. 101. Section through the margin of the optic cup of a foetus of 153 mm. (after Bach and Seefelder). *M.S.*, marginal sinus; *S.*, first appearance of fibres of sphincter pupillae within the cells of the wall of the marginal sinus. Outer layer is shewn above, inner below.



Fig. 102. Section through the margin of the optic cup of a 180 mm. human foetus. Outer layer above, inner below. Developing sphincter shewn in blue, pigment granules brown. The marginal sinus is larger than in the preceding stage seen in Fig. 101 (after Bach and Seefelder).

Digitized by Illinois College of Optometry Library

the muscle occur here and there and are known as *Fuchs' spurs.* Figs. 98 and 99 shew these spurs of both kinds in a 5 months foetus. The muscle at this stage is solid, unpigmented and quite avascular. It is closely in contact with the iris epithelium. At 6 months the first appearance of mesodermal derivatives can be recognised. These take the form of fine connective tissue septa containing capillaries, which invade the muscle bundles and finally separate them completely from the parent ectoderm. These can be easily recognised by 7 months.

Fig. 103 shews the appearance of the sphincter region in a 7 months foetus in which the blood vessels had been injected with

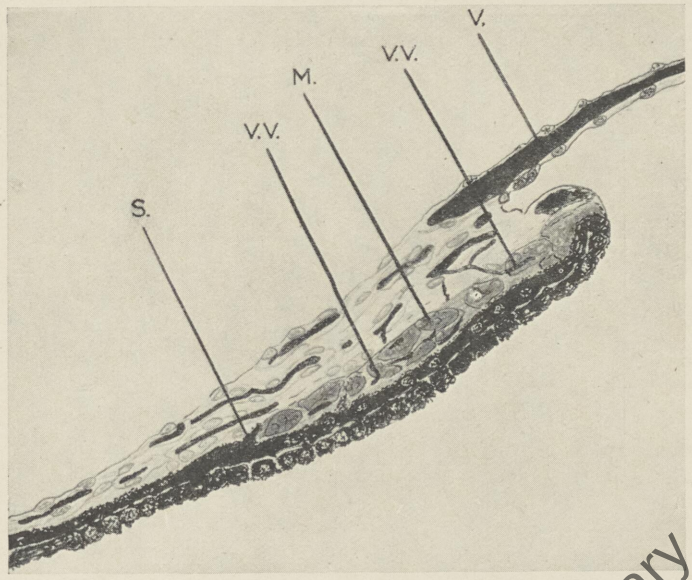


Fig. 103. Section through the iris of a 7 months human foetus (230 mm. approx.). *S.*, Michel's spur; *V.V.*, small vessels penetrating the sphincter mass; *V.*, large superficial vessel of the pupillary membrane; *M.*, sphincter pupillae.

Indian ink. It will also be noted that at this stage pigmentation of the posterior layer of the epithelium is complete up to the root of the iris. The muscle bundles can be seen with the capillaries growing in between them from branches of the large vessels of the iris stroma. Fig. 104 shews a low power view of the iris and ciliary region in this foetus. The section passes almost through the bottom of the valley between two ciliary processes, so that the process shewn does not appear as large as those in Fig. 98.

The sphincter pupillae is practically complete by the 8th month and is undoubtedly capable of functioning long before this. Indeed it is possible that a direct reaction to light would take place during the

Digitized by Illinois College of Optometry Library

4th month, since muscle fibres in a primitive condition (i.e. still in continuity with ectoderm) are present at this time and are possibly more directly irritable than later when a definite nerve supply is established.

The **dilatator pupillae** begins to develop at 6 months, long after the sphincter is clearly distinguishable. There has been some difference of opinion as to whether the muscle fibres come originally from the sphincter mass and grow peripherally as a very thin layer over the surface of the anterior epithelial layer, or whether they develop from the cells of this surface *in situ*. From the work of later observers, including Seefelder, whose observations appear conclusive

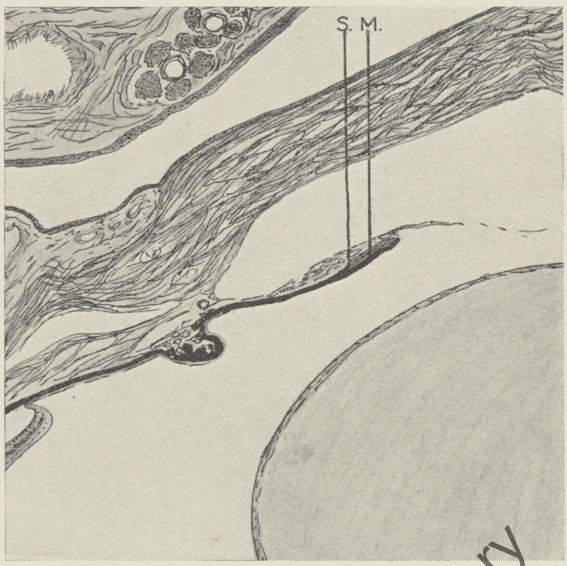


Fig. 104. Low power view of iris and ciliary region in a 6 months human foetus. *M.*, sphincter pupillae; *S.*, Michel's spur.

for man, it is probable that the latter view is correct. Fig. 105 shews the earliest recognisable change in the cells of the anterior layer peripheral to Michel's spur. The condition extends to the root of the iris. The cells involved are the short columnar cells of the anterior layer of the epithelial iris and the change consists of the appearance of fine longitudinal striations, parallel to the plane of the iris, in the anterior third of their protoplasm. The nuclei lie in the posterior parts of the cells. These striations increase in number until birth when they form a definite layer in intimate contact with the iris epithelium. Indeed the layer made by them does not appear truly separated from this at any time, and never seems to contain nuclei, so that the dilatator can be looked upon as formed by a direct

Digitized by Illinois College of Optometry Library

transformation of the protoplasm of the anterior parts of the cells of the anterior layer of iris epithelium. Pigment grains can be seen

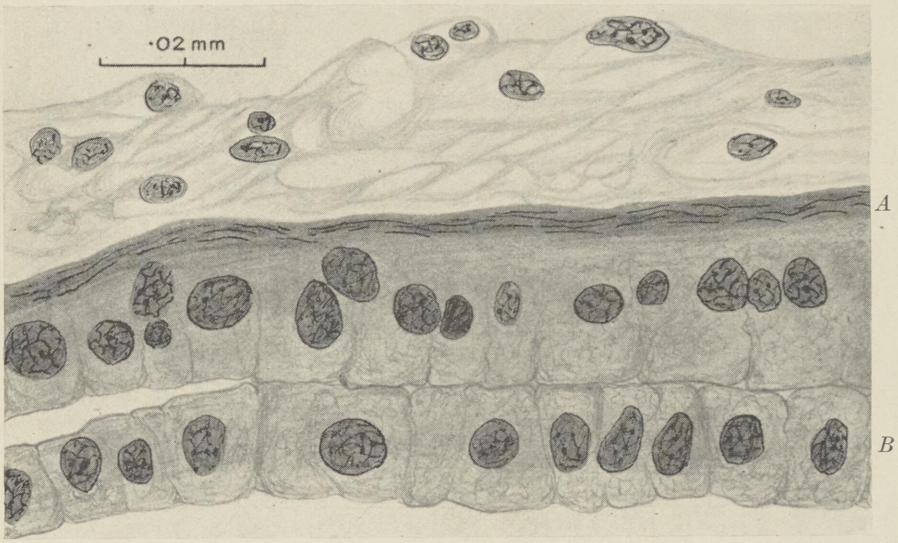


Fig. 105. Section through both the epithelial layers of the iris in a bleached specimen from a foetus of 6 months (after Bach and Seefelder). *A*, outer or anterior layer with developing longitudinal striations; *B*, inner or posterior layer.

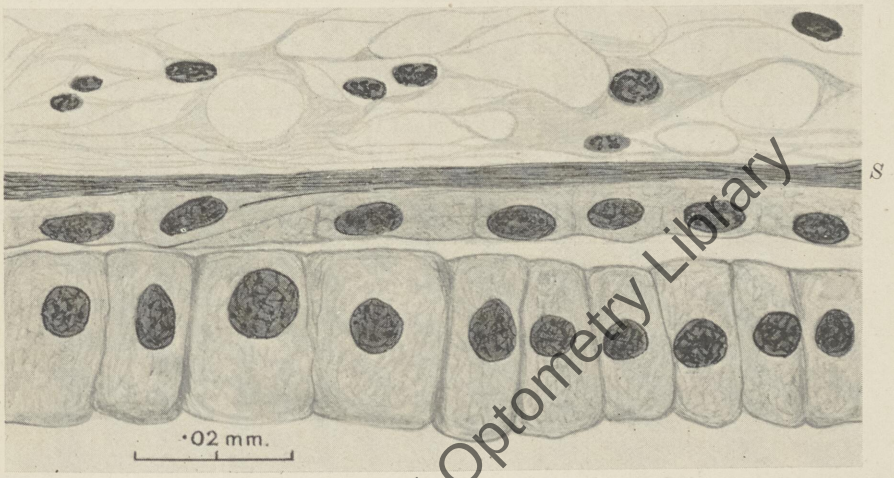


Fig. 106. Section through the epithelial layers of the iris at birth (after Bach and Seefelder). The specimen is bleached. The dilatator pupillae fibres are seen as an intracellular layer on the surface of the anterior epithelial layer at *S*.

among the striations. *The dilatator never becomes vascularised nor does any mesoderm ever grow between it and the ectoderm.* It thus differs from the sphincter by remaining in a more embryonic state.

Digitized by Illinois College of Optometry Library

Fig. 106 shews the condition which at birth extends from Michel's spur peripherally to the root of the iris.

The size of the pupil during development. The study of the size of the pupil during development affords a certain amount of information as to the growth rates of the various regions of the optic cup. Fig. 107 represents in a graph the actual growth rates of certain of

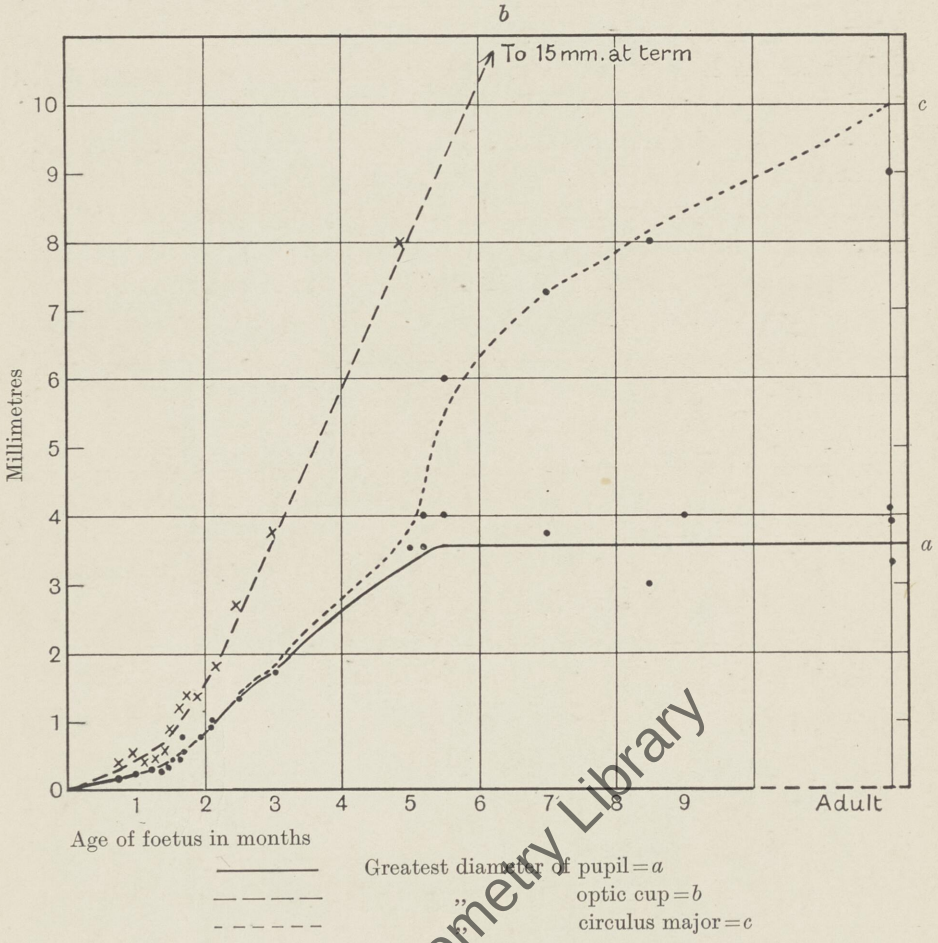


Fig. 107. Graph shewing growth rates of various parts of the eye.

them and Fig. 108 two ratios which can be deduced from these. In Fig. 107 measurements in millimetres are plotted against the age of the foetus. Three series of measurements are shewn. The interrupted line on the left shews the greatest equatorial diameter (measured between the outer surfaces of the pigment layers) of the optic cup. It will be seen that at first increase in diameter is slow. This is most marked up to the 5th week and corresponds with the period

Digitized by Illinois College of Optometry Library

during which invagination of the vesicle to form the cup is occurring. It is a period of orientation and large differentiation rather than of growth and is marked by a change of shape without much increase in size. After the 5th week growth in size is rapid and maintains a perfectly uniform rate until the 7th month, after which it slows down slightly.

The *second* (dotted) line shewn in Fig. 107 represents the diameter of the major circle of the iris. The vessel is taken as it affords a relatively fixed point outside the eye with which the position of the

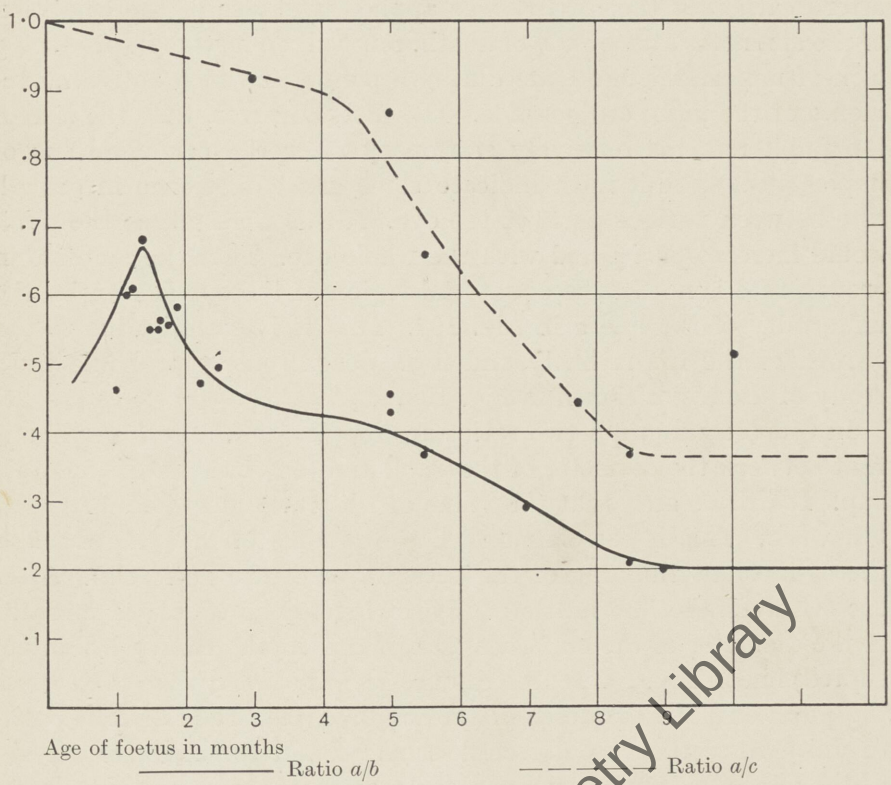


Fig. 108. Graph shewing the ratios a/b and a/c deduced from Fig. 107.

margin of the optic cup can be compared. The line shewing its increase diverges somewhat (i.e. marks a less rapid increase) from the line of the diameter of the whole cup owing to the fact that this latter changes its shape from a slightly elongated cup-like form to a sphere and therefore the diameter will, during this change, increase slightly in advance of the general growth rate of the embryo. The diameter of the major circle takes on a more rapid increase after the 5th month when differentiation of the anterior parts of the eye is proceeding apace.

Digitized by Illinois College of Optometry Library

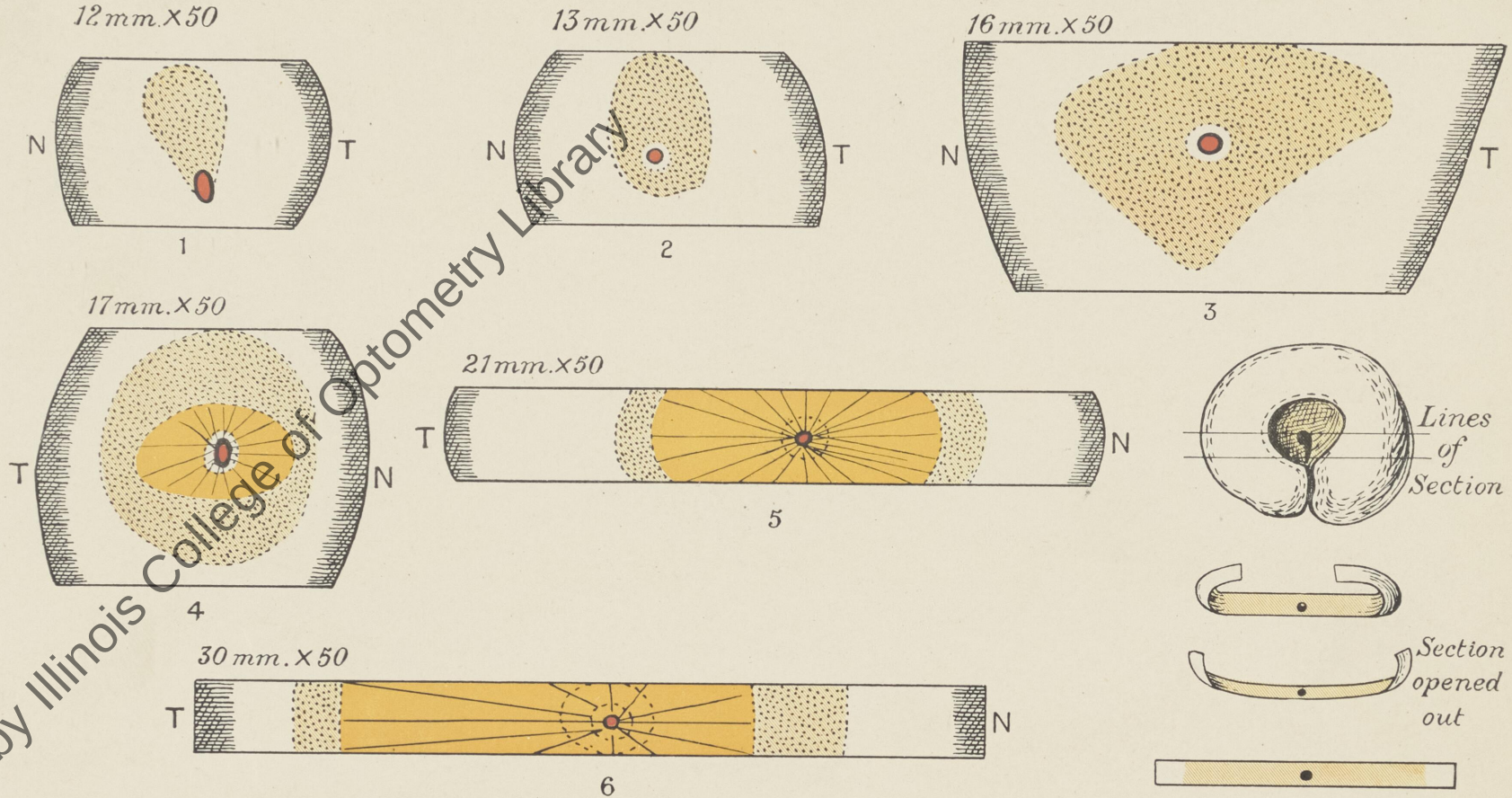
The *third* line represents the diameter of the pupil. It will be seen that up to the 5th month this line rises steadily at a rate at first exactly the same as, and after the 3rd month a little less than, that representing the diameter of the major circle (which can be taken roughly to indicate the growth rates of surrounding structures and possibly of the whole embryo). After the 5th month the diameter of the pupil scarcely alters at all if an average of several measurements is taken. Individual measurements are not of so much value after the 5th month, since the questions of fixation, of length of time after death that the fixative was applied, and also of the condition of the sphincter at the time of death, must all be factors in producing lack of uniformity of results during a period in which active movements of the pupil are possible. The fact, however, that the size of the pupil remains relatively stationary after the 5th month is of importance, since it must indicate some great difference in growth rate between various parts of the eye. If this were not so the pupil would increase *pari passû* with the whole eye. That the increase in growth rate is not in the equatorial region of the eye is seen by the uniformity of the line *a* in Fig. 107. That it is directly due to the growth of the iris is likely and is made extremely probable by a study of the ratios shewn in Fig. 108.

In this second graph two ratios are represented. The *lower* line is that between the diameter of the pupil and the diameter of the optic cup. It will be seen that the value of this ratio increases up to the 6th week. This is correlated with the process of invagination and the co-incident thinning of the outer layer of the optic cup. After the 6th week the line falls steadily, owing to the excess of increase of the diameter of the cup over that of the pupil. The *upper* (interrupted) line in Fig. 108 represents the ratio between the diameter of the pupil and the diameter of the major circle. It is at first equal to unity since the vascular circle runs around the extreme margin of the cup. As growth proceeds, the margin of the cup comes slowly to extend just in front of the vessel, so that by the 4th month the ratio has fallen to 0·9. After this, growth of the iris begins, and co-incidentally the ratio falls rapidly until $8\frac{1}{2}$ months when the iris is complete, after which it remains stationary. This serves to make clear the fact that it is the more rapid growth of the margin of the optic cup than of the equatorial region which is mainly responsible for the fact that the pupil decreases in relative size while increasing in absolute.

The differing rates of growth of the various regions of the optic cup can also be understood by studying the mode of spread of

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library



Digitized by Illinois College of Optometry Library

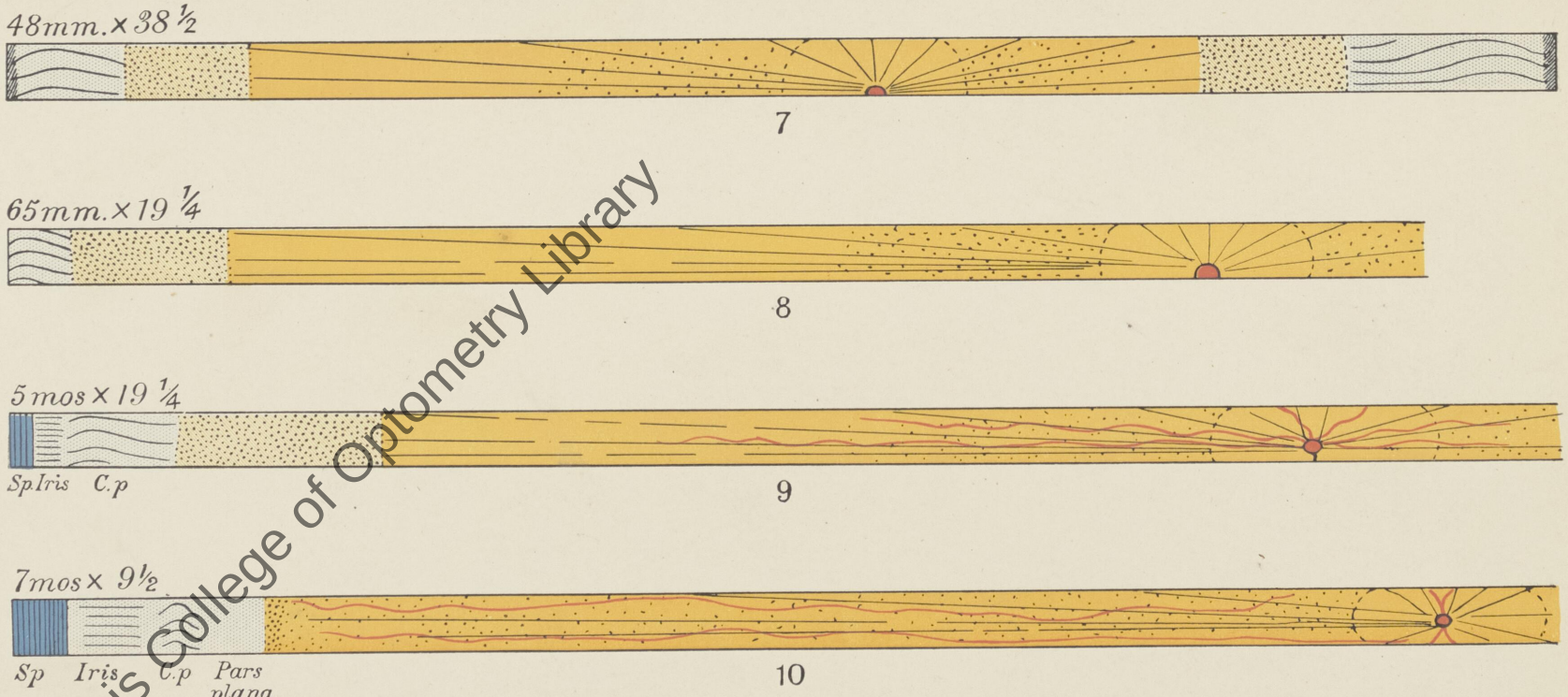


FIG. 109. DIAGRAMMATIC REPRESENTATION OF THE PROCESS OF DIFFERENTIATION OF THE WALLS OF THE OPTIC CUP.

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

differentiation. We have already seen that this is always from the posterior pole forwards, i.e. from the older (ontogenetically and phylogenetically) to the newer regions.

Fig. 109 shews a series of reconstructions of the retinal surface of eyes of human embryos of various ages. The small diagram on the right explains the method of reconstruction. A thick horizontal section is taken through the region of the disc and is spread out flat. The first scheme shews the posterior pole of a 12 mm. eye (retina shewn in Fig. 67). The dotted area extending above the epithelial papilla represents the area over which migration of nuclei inwards into the marginal layer is taking place (i.e. the region of inner and outer neuroblastic layers). The area outside this represents the region over which the marginal layer is free from nuclei, while the narrow shaded band at the extreme periphery represents the growing edge where the wall of the cup has the character of a simple neuro-epithelium only, even the marginal layer being absent.

No. 2 shews the same region in a 13 mm. human embryo. The most important and essential difference is that the area over which nuclei are migrating into the marginal layer (inner neuroblastic layer) now extends below the epithelial papilla, the fissure having closed here, the orifice of the papilla being in consequence circular and not oval as in the previous scheme.

In No. 3 (16 mm.) this area has extended still farther and in addition the whole eye is larger.

In No. 4 (17 mm.; see Figs. 70 and 71) the area of the two nuclear layers is almost circular, with the papilla in the middle, and in addition a new region has appeared (marked by radiating lines), i.e. the area over which nerve fibres can be recognised. This extends farther above the disc than below, thus following at its first appearance the procedure of the migrating cells (inner neuroblastic layer) seen in 1 and 2, which also extend at first farther above the papilla than below. The densely cellular zone at the edge of the cup can be seen as the shaded area in the periphery. The area between this and the dotted region still retains the primitive arrangement of cellular layer and marginal layer only.

From now onwards differentiation spreads radially from the disc, the appearance of inner and outer neuroblastic layers always preceding that of the nerve fibre layer, and the area where differentiation into cellular and marginal layers alone is present decreasing in width both relatively and absolutely, until at 48 mm. it has disappeared entirely, the two neuroblastic layers extending right up to the simple epithelium of the future ciliary region, which never develops a marginal layer.

Digitized by Illinois College of Optometry Library

In No. 5 (21 mm.; see Figs. 72 and 73) the increase in nerve fibres can be seen.

In No. 6 (30 mm.) this increase is more marked and is shewing a narrower nucleus-free marginal layer.

In No. 7 (48 mm., Figs. 74 and 75) this can no longer be recognised. The undifferentiated region of the edge of the cup is increasing rapidly, since it is at this stage that the margin of the cup begins to grow more rapidly in proportion to the rest, to form the ectodermal part of the iris and ciliary body. At 65 mm., No. 8 (see Figs. 34, 77 and 78), a great increase in the size of the whole eye is apparent, otherwise the areas remain relatively about the same.

At 5 months, No. 9, beyond increase in size of the whole eye the most striking change is in the relative and absolute increase in the size of the ciliary and iridic regions. The iris can be readily distinguished from the ciliary processes and the developing sphincter seen. There is no pars plana as yet.

By 7 months, No. 10, the iris with its sphincter, the ciliary processes, the pars plana, and the pars optica retinae can all be distinguished, the main difference from the adult state being in the fact that the nerve fibre layer does not extend as yet quite up to the ora serrata.

Thus it is clear that growth is at first more active at the posterior pole, and that only after differentiation is well advanced here does the region of the margin of the cup begin to exhibit active change.

D. The Optic Nerve (and Chiasmal Region)

The *optic nerve* is developed in the substance of the *optic stalk*. The cells of the stalk itself, however, merely form the neuroglial supporting tissue of the optic nerve, the actual nerve fibres being developed from the ganglion cells of the retina (i.e. cells of the inner layer of the optic cup). The nerve sheath and the connective tissue around the central vessels, and the septa connected with this, arise from surrounding mesoderm, some of which condenses on the outside of the stalk, while some accompanies the vessel when the stalk becomes invaginated.

The *optic stalk* can be recognised from the time that an optic vesicle is present. It is at first circular in section, relatively very short and thick, and having a large lumen continuous with the cavity of the fore-brain proximally and the cavity of the optic vesicle distally. Fig. 110 shews a model of the anterior end of the central nervous system at this stage (4 mm.). The optic stalk shares in the process of invagination. When this begins, the stalk is very short

Digitized by Illinois College of Optometry Library

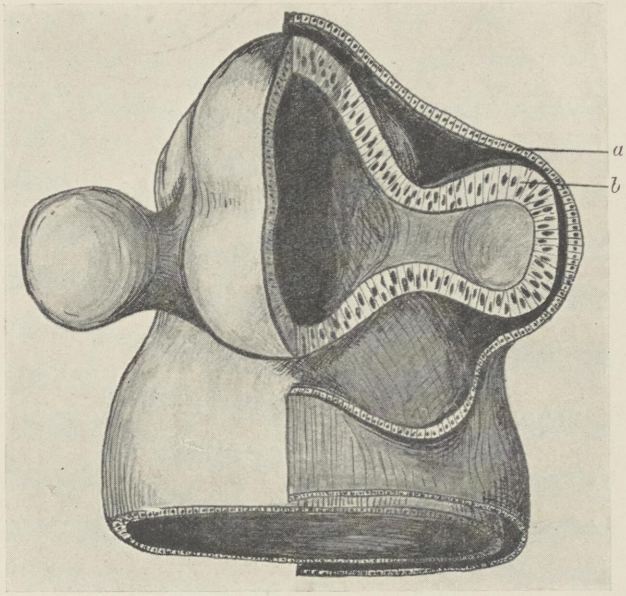


Fig. 110. Model of fore-brain and optic vesicles of a 4 mm. human embryo seen from the front. The optic vesicle on the left of the embryo is represented in section. *a*, surface ectoderm; *b*, neural ectoderm.

and a shallow depression is formed along its under surface throughout its whole length. This depression fades away on the under surface of the fore-brain. It can be seen in Fig. 111. As the stalk elongates

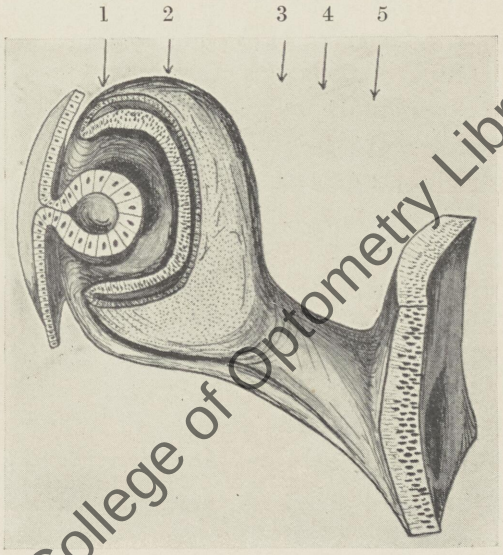


Fig. 111. Model of optic cup of 7·5 mm. human embryo. The wall of the cup has been partly cut away to shew the two layers.

Digitized by Illinois College of Optometry Library

the depressed area deepens in its distal part. It does not lengthen coincidentally with the stalk, but begins to fade away before it

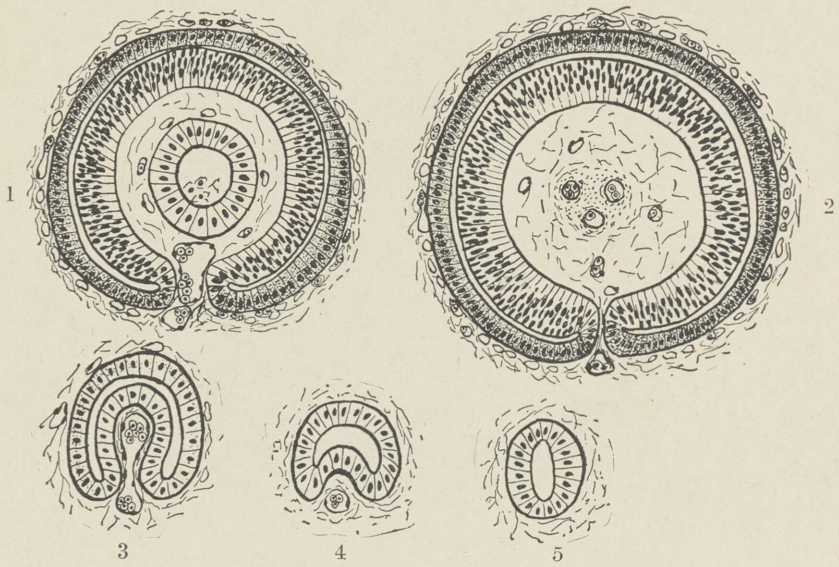


Fig. 112. A series of transverse sections through the optic cup and stalk of the eye seen in Fig. 111. The sections pass through the points indicated by the arrows.

reaches the brain, so that a slightly later stage shews an optic stalk which is crescentic on section near the optic cup and circular near the brain. Fig. 112 shews a series of transverse sections through such a stalk, making the gradual change of outline clear. The invagination deepens to form a groove as it is followed outwards and this is occupied by a blood vessel (which eventually becomes the intraneural portion of the *arteria centralis retinae*).

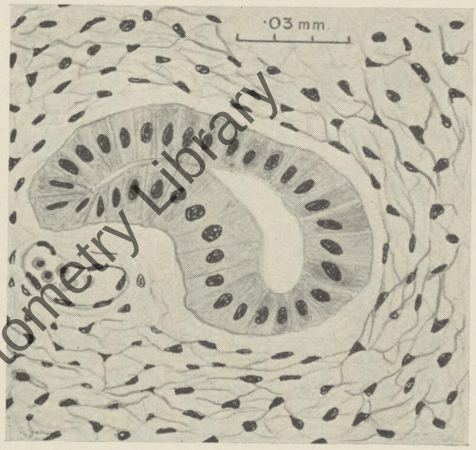


Fig. 113. Transverse section through the optic stalk of a 13 mm. human embryo. The vessel in the concavity of the stalk is the hyaloid artery.

Before the appearance of nerve fibres in the inner layer of the optic cup the wall of the stalk is composed of an undifferentiated neuro-epithelium. Fig. 113 shews a transverse section through the stalk of a 13 mm. human embryo. The lumen has by this time become very small and the stalk itself is very thin.

Digitized by Illinois College of Optometry Library

With the appearance of nerve fibres in the retina a change takes place in the inner layer of the optic stalk, commencing at the distal end, i.e. in that portion which is continuous with the inner (nerve-fibre-bearing) layer of the cup. The cells become somewhat irregularly arranged and vacuoles appear in them. At the same time axis cylinders from the retina grow in among these vacuolated cells,

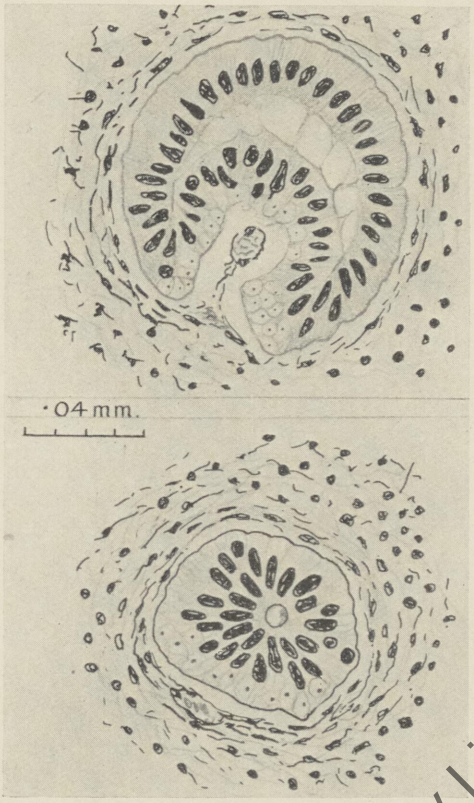


Fig. 114. Two sections through the optic stalk of a 17 mm. human embryo. *A* is taken just behind the cup, *B* a little more than halfway along the stalk towards the brain.

which disappear as the nerve fibres increase in number and replace them. Fig. 114 shews two transverse sections through the optic stalk of a 17 mm. embryo, the retina of which is shewn in Fig. 71. The upper section is taken just behind the cup, and shews the invagination of the stalk, the hyaloid artery lying in the concavity, and the appearance of vacuoles and axis cylinders in the cells immediately bounding this. The lower section is taken a little more than halfway along the stalk towards the brain and shews a circular outline with nerve fibres visible in the lower part. A slight condensation in the

Digitized by Illinois College of Optometry Library

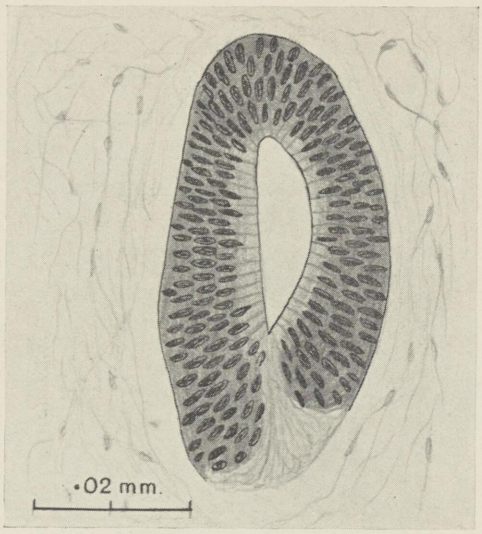


Fig. 115. Section through the optic stalk of a dogfish (Acanthias) embryo shewing nerve fibres in the lower part.

surrounding mesoderm is appearing as the precursor of the nerve sheath. At this stage the nerve fibres extend just up to the brain but cannot be recognised with certainty in the chiasma.

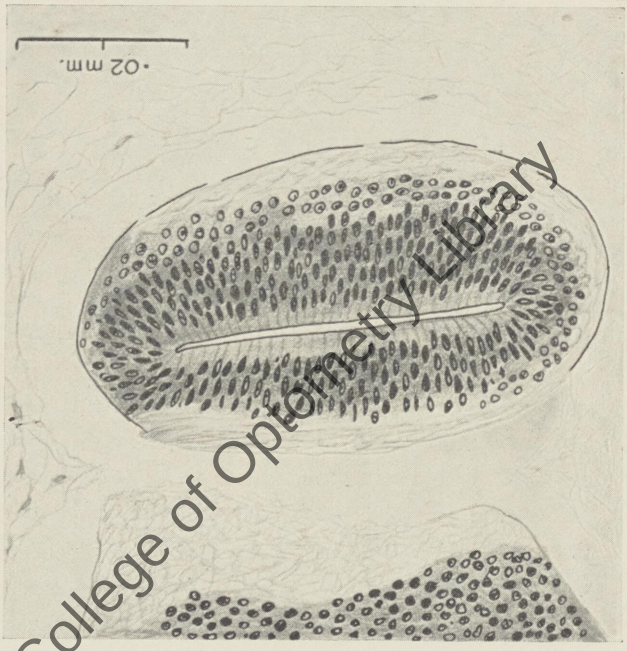


Fig. 116. Section across the chiasma of the same dogfish embryo as Fig. 115, shewing a central narrow cavity in it and the presence of nerve fibres on its lower surface.

Digitized by Illinois College of Optometry Library

Fig. 115 shews a slightly more advanced stage in a dogfish. The nerves fibres are all crowded together in the lower part of the stalk.



Fig. 117. Transverse section of the optic nerve of a 19 mm. human embryo (after Bach and Seefelder). Both layers of the stalk, the remains of its cavity and the hyaloid artery can be seen.

There are more of them and they reach the brain, as seen in Fig. 116, which shews them on the surface of the chiasma.

Digitized by Illinois College of Optometry Library

In human embryos the nerve fibres almost completely fill the stalk by 19 mm., as seen in Fig. 117. A small portion of the lumen is still visible and the margins of the cleft have come together as they do in the optic cup, so that the hyaloid artery is now completely encased in the nerve. The beginning formation of the glial septa can be seen, the cells of the outer layer of the stalk taking part in this.

By 25 mm. the stalk is completely filled with nerve fibres and no trace of lumen can be seen. Most of the cells of the original stalk can be seen as glial cells arranged in longitudinal rows between the

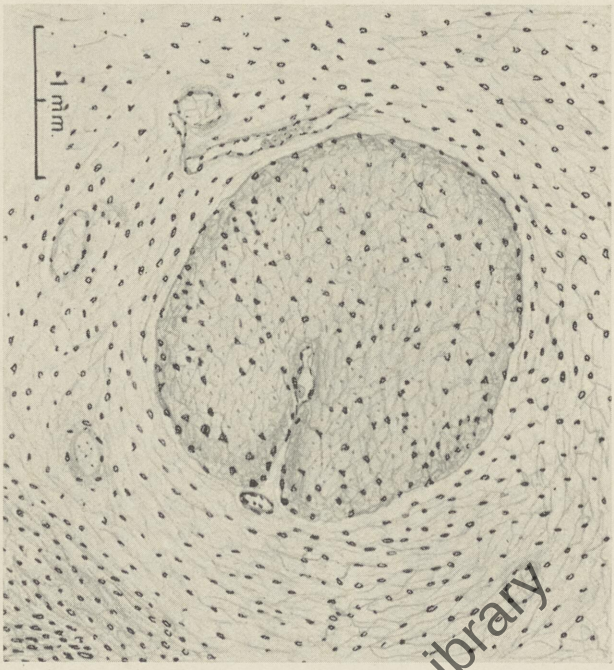


Fig. 118. Section through the optic nerve of a 25 mm. human embryo.

bundles of nerve fibres. Fig. 118 shews a somewhat oblique section through such a nerve. The mesodermal sheath will be seen to be much more advanced. The nerve increases from now onwards *pari passû* with the retina and closely resembles the adult nerve, save that the fibres have as yet no medullary sheaths. Fig. 119 shews the optic disc of a 5 months eye. It will be seen to resemble that of the adult except that the hyaloid artery projects from its centre into the vitreous. Other than the retrogression of this and the increase in size, the nerve undergoes very little change until the fibres become medullated. The exact time of this has been the subject of some difference of opinion, some authors giving it as

Digitized by Illinois College of Optometry Library

before birth, others at the 9th month only. It is possible that individual variations may occur in this since the amount of general development at birth is not absolutely constant. The investigations of C. H. Sattler are of value in deciding the point. He examined a series of human foetuses from $5\frac{1}{2}$ to $10\frac{1}{2}$ lunar months (27–59 cm.) and found that the medullation commenced in the central nervous system and spread peripherally along the nerve. There was no

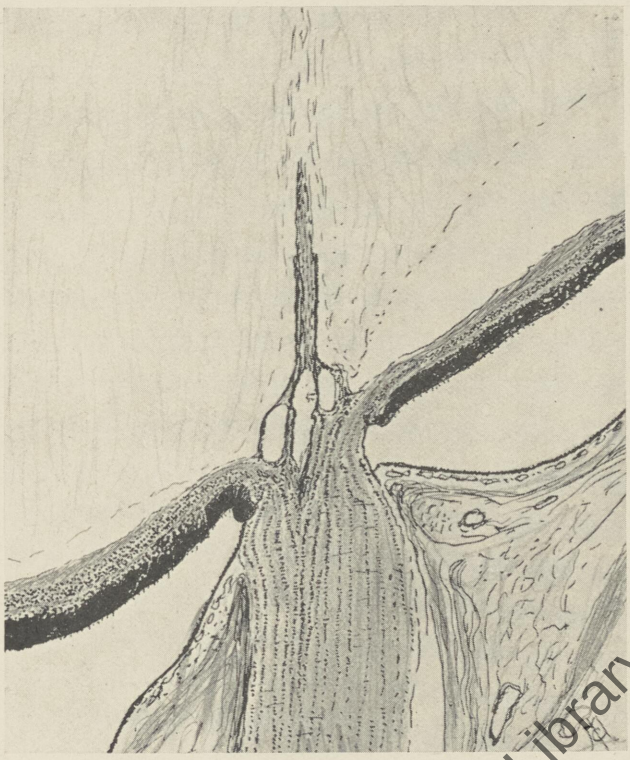


Fig. 119. The optic disc at 5 months. Note the hyaloid artery with its glial sheath projecting from the centre into the vitreous.

medullation at all at 5 months. In the 37 cm. (circ. 7 months) foetus medullary sheaths could be traced from the optic tract to the beginning of the optic nerve and by term these had reached the *lamina cribrosa*. The medullation appears first as minute droplets of a lecithin-containing substance in the protoplasm of the glial cells. These droplets run together and surround the axis cylinders. The sheaths are at first very thin, and as development proceeds they thicken proximally at first, so that at birth the medullary sheaths in the optic tract are thicker than those in the nerve behind the eye, whereas in the adult they are the same thickness.

Digitized by Illinois College of Optometry Library

The region of the chiasma can be recognised, as soon as the optic vesicles have grown out of the nerve tube, as that portion of the floor of the fore-brain which lies between the insertions of the optic stalks. It is of course entirely epithelial in structure at first and, when looked at from below, shews merely a smooth convexity lying in front of the region where Rathke's pouch comes in contact with the floor of the fore-brain. As development of the central nervous system proceeds, this convex region, which is hollow, projects more and forms a definite ridge uniting the two optic stalks. Their lumina open into its cavity, which can now be called the *recessus opticus*. This recessus deepens and its wall undergoes differentiation in common with the rest of the wall of the

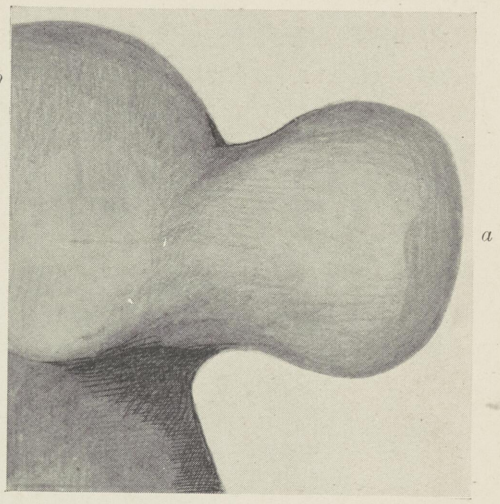


Fig. 120. A portion of a model of a 4 mm. embryo, shewing one optic vesicle and the fore-brain seen from below. *a*, optic vesicle; *b*, fore-brain; *c*, region of future chiasma.

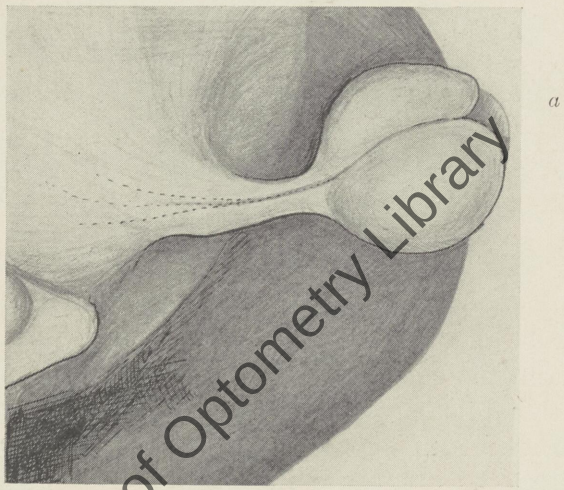


Fig. 121. Reconstruction of the chiasmal region and eye of a 12 mm. human embryo. *a*, eye; *b*, Rathke's pouch.

fore-brain, until distinct ependymal, mantle and marginal zones can be recognised at 12 mm. Further cellular differentiation does not occur, since soon after this the marginal layer begins to get filled up with

Digitized by Illinois College of Optometry Library

nerve fibres growing into it from the lower surface of the optic stalk. Fig. 120 shews the appearance of the region under discussion in a 4 mm. human embryo. There is no differentiation of the wall at this stage (see Fig. 14 for a transverse section of this stage). Fig. 121 shews the appearance from below in a 12 mm. embryo. The recessus opticus is deeper and so appears as a more definite ridge on the outside. At this

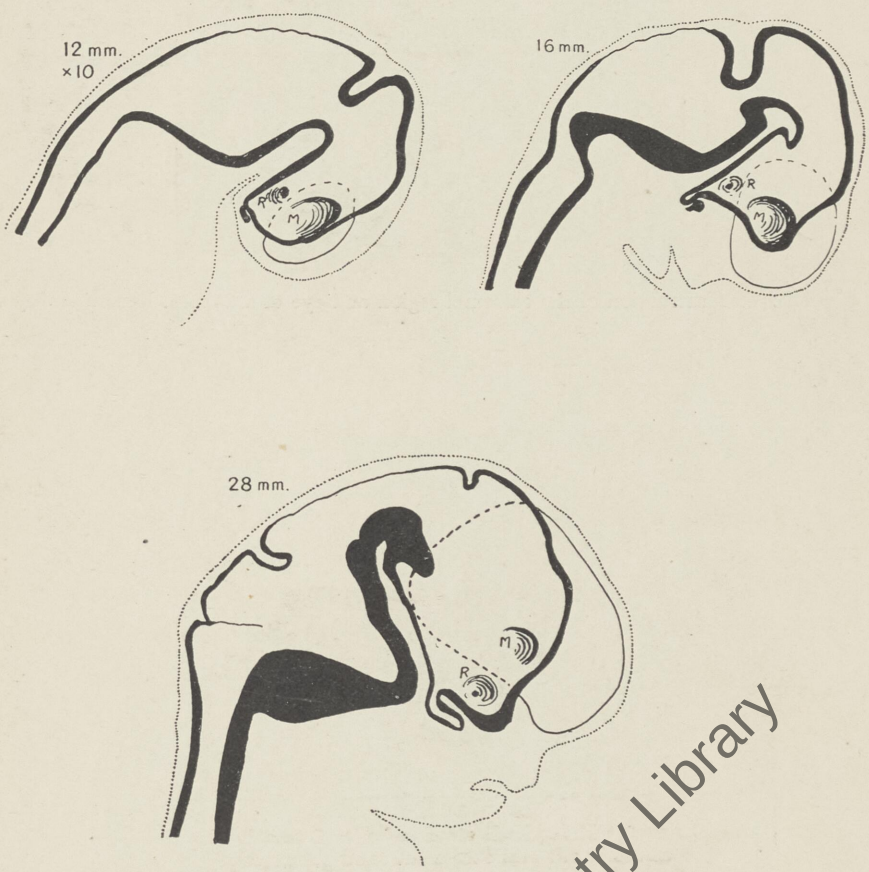


Fig. 122. Median sagittal sections of human brains from embryos of 12, 16 and 28 mm. *R*, recessus opticus; *M*, opening into cerebral vesicle.

time the wall of the recess shews a wide superficial marginal layer, into which the nerve fibres grow at 18 mm. It can be seen from Fig. 121 that there is a direct path along the surface from the inner layer of the optic cup through the open upper end of the choroidal fissure into the inner layer of the stalk and thence along its under side on to the under surface of the fore-brain in front of the pituitary region. This path for the nerve fibres is marked in Fig. 121 as a series of dotted lines, but it must be realised that they do not follow it until

Digitized by Illinois College of Optometry Library

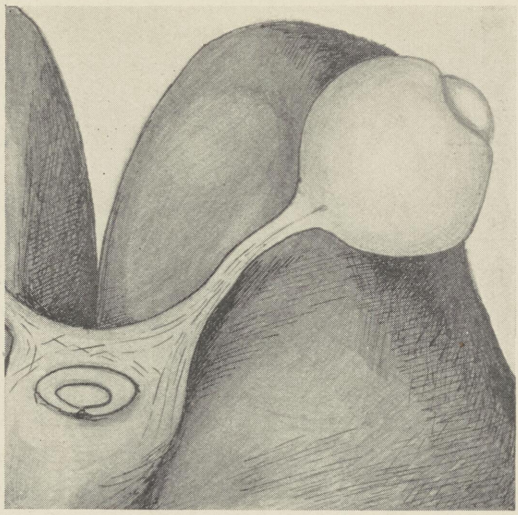


Fig. 123. Reconstruction of the chiasmal region and eye of a 25 mm. human embryo.

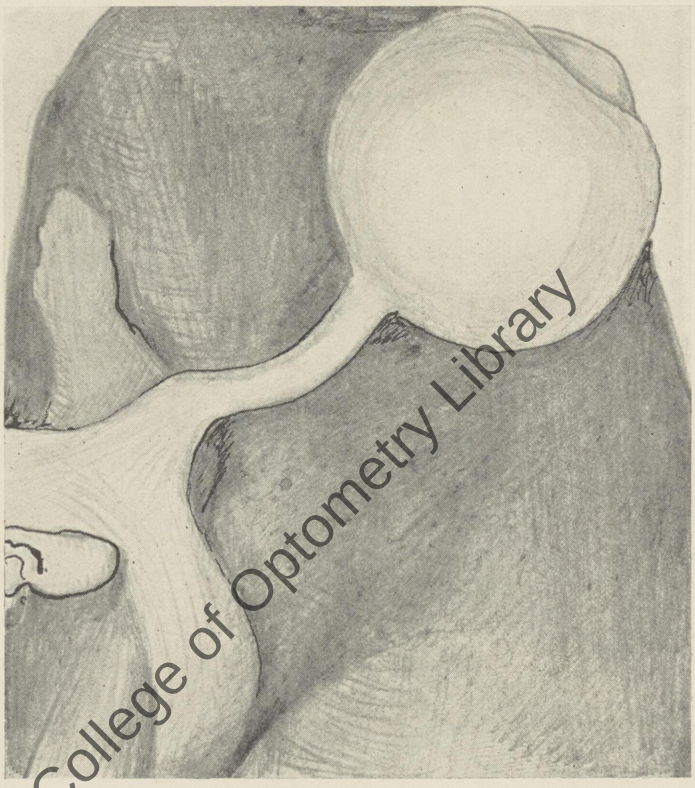


Fig. 124. Chiasmal region in a 48 mm. human embryo.

Digitized by Illinois College of Optometry Library

about 18 mm. At 12 mm. there is naturally no sign of the optic tract, since this is formed by the nerve fibres themselves, while the convexity in the future chiasmal region is originally due to the downward projection of the fore-brain (on each side of which are the optic outgrowths). Fig. 122 shews a series of median sagittal sections of developing brains in which this deepening of the optic recess can be seen.

By 25 mm. the nerve fibres are well developed and cover the surface between the two optic stalks, so that a true chiasma may now be spoken of. The fibres, after partially decussating in the chiasma, now pass backwards round the base of the pituitary body, and a definite convexity can be recognised in the situation of the optic tract. Fig. 123 shews the view from below in this region in a 25 mm. embryo. The process of deposition of fibres on the surface continues, so that by 48 mm. the appearance is that seen in Fig. 124, where the adult arrangement can already be made out. Fig. 125 shews a 4 months brain seen from below, shewing that, although the olfactory area is still far from the definitive condition, the optic chiasma and tract are practically complete. As stated above, medullation of the fibres can be recognised in the tract first at 37 cm., whence it spreads to the chiasma and nerve.

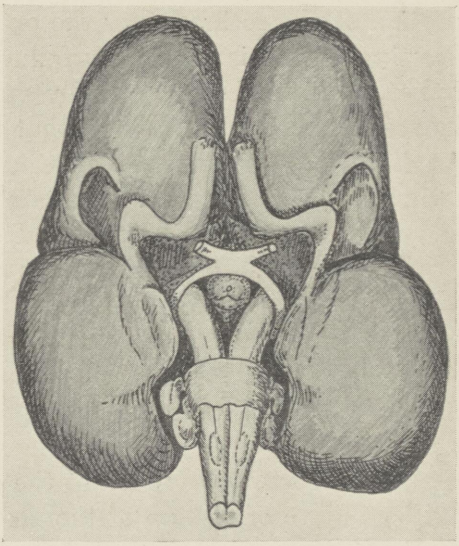


Fig. 125. The brain of a 4 months human foetus seen from below. Note that the optic chiasma and tract present already the adult arrangement while the olfactory tract and cortex are still rudimentary (after Keibel).

Abnormalities

Certain abnormalities of development may arise during differentiation of the walls of the primary optic vesicle. The most important of these may be grouped roughly into those which imply an anomaly of shape of the optic cup and those which are manifest merely as local or general abnormalities of histological structure, the form and size of the eye being normal.

Digitized by Illinois College of Optometry Library

In the first group *typical coloboma retinae* is the most arresting anomaly met with[1] and has aroused the most speculation. It cannot be said even now that the causation and mechanism of production is completely understood, and it is probable that several different types occur, each produced in a slightly different way.

The fact that the abnormality most commonly involves that portion of the retina below the optic disc has given rise to the impression that it is caused by failure of closure of the foetal fissure. It has, however, been shewn by very many observers (Szily, Hess, Koyanagi, Mayou and others) that there is no true gap in the retina. An intercalary membrane continuous with and derived from the retina is always present. The gap is really in the chorio-capillaris and other layers of the choroid. The structure of the retina in the gap is atypical. Pigmentation is absent in the outer layer. The nuclei are thinned and generally absent altogether in the central parts in the inner layer. But in some cases both inner and outer layers shew three bands of nuclei and even abortive rods and cones, the outer layer with inverse arrangement. These facts, together with a study of the embryology of the condition in rabbits, in which it is often hereditary, have led to the conclusion that it may be caused not by failure of closure of the fissure but by excessive eversion of the inner layer of the cup before closure, so that a portion of the inner layer remains outside over an area of varying size at the posterior pole. It can be shewn that normally the chorio-capillaris layer of the choroid only develops from mesoderm which is in contact with pigmented epithelium. The mesoderm in contact with the cauda of the nerve in birds does not give rise to chorio-capillaris nor, of course, does the mesoderm in contact with the inside of the optic cup. In the same way, apparently, no chorio-capillaris will develop when mesoderm is in contact with an abnormally everted portion of the inner layer of the cup. Hence it is absent over a coloboma, and the resulting failure of nutrition may explain the loss of function and extreme atrophy of the retina in this region. The retinal vessels themselves usually pursue their normal course, so that there is no lack of nutrition from the inside.

Various hypotheses to explain the excessive eversion of the inner layer have been advanced. It has been suggested that it is always associated with delay in closure and that this delay may be caused by the presence of mesoblast between the lips of the foetal fissure. In a certain number of cases this is rather borne out by the per-

[1] Anophthalmia, congenitally cystic eye and microphthalmia with cysts have been mentioned in Section II.

Digitized by Illinois College of Optometry Library

sistence of other mesoblastic structures beyond their normal time in eyes with coloboma retinae, e.g. persistent pupillary membrane and hyaloid artery, though as to the initial cause of such persistence we know very little. It seems best that typical coloboma of the choroid be considered as due to an arrest or delay of development of the lower part of the optic cup, associated with aberrant growth of the margins of the foetal fissure, and sometimes with thinning of the sclera. It probably cannot be considered atavistic, although it is an anomaly of the phylogenetically youngest part of the eye. It is true that in certain birds the fissure never closes completely, but this is a secondary modification called for by the peculiar vascular conditions in the bird's eye and is not a primitive characteristic.

Colobomata may also occur in other regions of the eye, but very little is known to account for this. Some observers have supposed a rotation of the eye so as to bring the cleft into the position of the coloboma, but, since a normal rotation is not now thought to take place, it seems unlikely that this is the true explanation. It is better not to consider such atypical patches of retinal and choroidal atrophy as having any connection with the cleft or with normal development at all. A certain number of them may be explained as the result of intra-uterine disease, while others are possibly due to haemorrhage at birth.

Abnormalities of shape of the anterior parts of the optic cup are also found. Of these the most important are *cysts of the iris*, *grape-seed bodies on the iris* and *adhesions of the ciliary processes to the lens capsule*. *Cysts of the iris* occur between the two layers of epithelium on the posterior surface of the iris. They can therefore be considered as dilatations of persisting portions of the cavity of the primary optic vesicle, and are possibly associated with failure of disappearance of the marginal sinus. Related to cyst of the iris are the formations known as *grape-seed bodies on the iris*. These are globular hollow proliferations of the walls of the marginal sinus which project beyond the pupil margin. The cavities communicate with that of the marginal sinus and, like it, can be looked on as persistences of the cavity of the primary optic vesicle. Such globular processes of the edge of the iris are normal in many of the lower mammals (horse, sheep, lion among others) and those in the human subject are probably developed in the same way.

Adhesion of the ciliary processes to the lens capsule is brought about by abnormal persistence of the condition found normally at the 5th month (see Fig. 47). This persistence leads to irregularity of development of the suspensory ligament, to dislocation of the lens,

Digitized by Illinois College of Optometry Library

and sometimes to abnormality in the shape of the lens. Occasionally the adhesions give way before birth, and their former site remains permanently marked by patches of pigment on the lens capsule in the equatorial and posterior regions.

Abnormalities of histological structure of the retina can take the form of localised patches of tissue which would be normal in other situations, such as pigment epithelium in the inner layer of the cup, nerve fibres in the outer layer or retinal cells on the optic disc. These may all be explained by the theory of the pluripotentiality of the cells of the primary optic vesicle (Coats). On the other hand, congenital anomalies of differentiation occasionally involve the whole retina. Many of these are only known clinically and the final histological proof is wanting. This is the case with congenital complete colour blindness and congenital night blindness, which from their symptoms alone can be postulated as a failure of production of cones or of rods respectively, the functional retinal elements being homogeneous in both cases but not similar. Very little is known as to cause, though attempts have been made to classify the conditions as examples of atavism. This may possibly be justified in the case of congenital complete colour blindness, since monochromatic vision is presumably the precursor of colour vision in phylogeny. Allied to these anomalies of differentiation is *Oguchi's disease*, in which histological corroboration is available. It has been shewn that in this congenital abnormality (which resembles night blindness, but has definite ophthalmoscopic signs) there is present motility of processes of the pigment epithelium similar to that found in many of the Amphibia and Sauropsida.

Other anomalies of differentiation may occur, such as the formation of small folds and puckers in the retina. These are common in microphthalmic and malformed eyes, and represent failure of complete coaptation of the inner to the outer layer of the optic cup. Abnormalities of medullation may occur. These, though developmental, are not truly congenital, since medullation has barely reached the lamina cribrosa at birth. In these cases it spreads beyond this on to the disc and, in irregular patches, on to the retina beyond this. This also is the normal condition in some of the lower mammals, notably the rabbit.

Another interesting anomaly of retinal differentiation must be described, since it affords a good example of an antenatal pathological process producing an apparent failure of development. This is seen in the retina of the *anencephalic* foetus, in which there is at first sight almost complete absence of ganglion cells and nerve fibres.

Digitized by Illinois College of Optometry Library

Fig. 126 shews the appearance at term. It will be seen that there are very few ganglion cells and that the nerve fibre layer is practically absent (so that the vessels lie on the surface). The outer layers of the retina are almost normal and the rods and cones developed. The condition therefore could not have arisen as an arrest of develop-

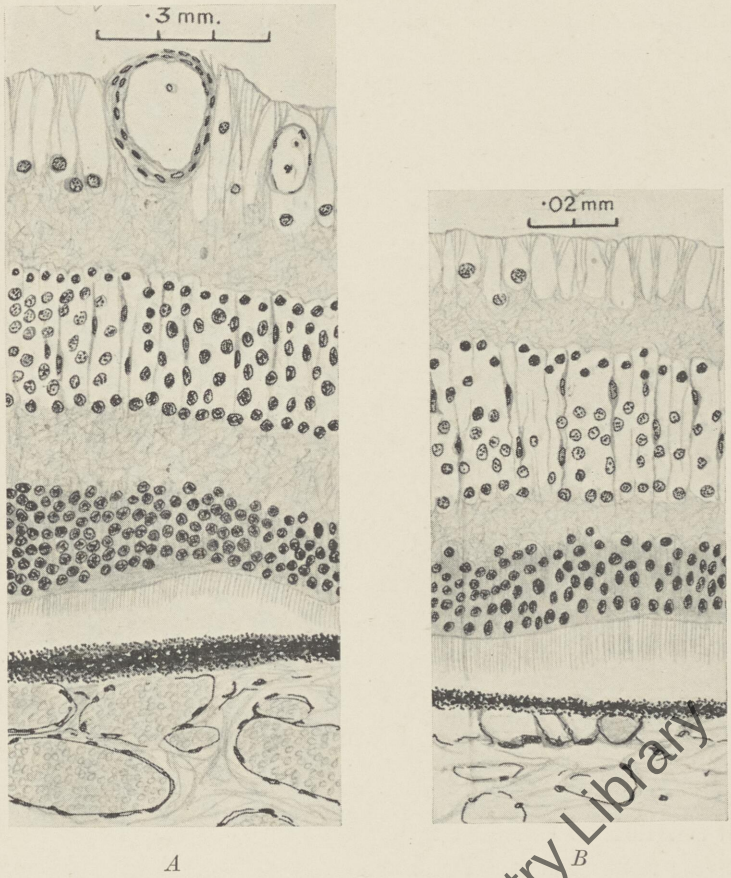


Fig. 126. *A* and *B* both shew sections through the retina of an anencephalic foetus at term. In *A* a blood vessel is seen lying at the surface of the retina. In *B* there is extreme atrophy of the nerve fibre layer and absence of ganglion cells.

ment, since the rods and cones differentiate after the ganglion cells and nerve fibres. Also it can be shewn by examination of the earlier stages of anencephaly that development of the eye is practically normal up to the time when ganglion cells and nerve fibres are appearing. Fig. 127 shews a section through the retina of a human embryo of the 28 mm. stage which exhibited the condition of anencephaly. This embryo has been described by Frazer, who is of the opinion that the primary defect of the brain tube was in the nature

Digitized by Illinois College of Optometry Library

of a rupture in the fore-brain region, possibly preceded by distension, and leading secondarily to rupture of nerves and vessels and consequent atrophy of structures above the site of the fault. The eyes were normal, though possibly not quite so advanced as usual at the 28 mm. stage, since the situation of the foetal fissure could still be appreciated at the margin of the cup. The figure however makes it apparent that ganglion cells and nerve fibres are present and that

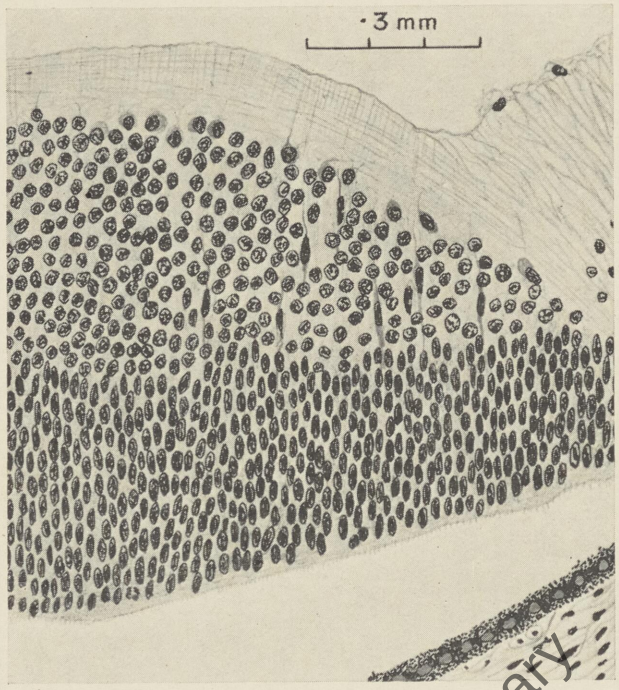


Fig. 127. Section through a portion of the retina near the disc in an anencephalic embryo of the 28 mm. stage. Ganglion cells and nerve fibres are present and differentiation is practically normal for the age.

differentiation of the retina is proceeding normally. The optic nerves ended blindly in the meninges just in front of the pituitary and there was no chiasma. A comparison of Fig. 127 with the condition of the retina seen in anencephaly at term (Fig. 126) makes it clear that the absence of the innermost layers in the latter is due to a secondary atrophy. Examination of this specimen affords important confirmation of the theory favoured by Parsons, namely that anencephaly is preceded by foetal hydrocephaly which leads to optic atrophy from stretching and finally rupture of the optic nerves.

Digitized by Illinois College of Optometry Library

V

THE VITREOUS AND SUSPENSORY LIGAMENT OF THE LENS

The problem of the origin of the vitreous is one over which the acutest of embryologists have disputed without intermission since the middle of the last century. The matter can scarcely be said to be settled to-day, since, although most observers are agreed as to the main sequence of changes which can be seen, they still differ as to their interpretation. It will therefore be realised that the subject cannot be approached in a dogmatic spirit.

The changes which occur in the walls of the optic cup and in the surrounding mesoderm can be easily seen and verified: no serious difference of opinion exists to-day concerning them. It is quite otherwise with the vitreous. We have not even a clear conception of its anatomical structure in the adult, and with the advent of improved methods of examination of the living eye (such as the slit-lamp and binocular microscope) it has become necessary to readjust many of our views on the subject. The reason for this uncertainty lies in the nature of the vitreous. It is a substance so delicate that its appearance may be profoundly modified by the slightest means, the chief among these being the kind of fixative employed and the time after death or removal of the eye that the fixative was applied. It is doubtful whether a microscopic section of the vitreous (or a fixed specimen of any sort) can ever give us a true idea of its nature and one which is consonant with what can be seen in the living eye. These objections apply more strongly still to embryonic material, where the slightest shrinkage or distortion may give rise to entirely misleading appearances of clefts, condensations, and other arrangements having no foundation in actual fact. It is doubtful whether the vitreous can really be regarded as a tissue, since it is practically acellular, and undergoes none of the usual tissue reactions to infection or injury. It appears to be more in the nature of a cell product, and a specific name, "membranine," has been given by Mörner to the substance composing it. The embryological problem is therefore to identify the cells which produce it, and, if possible, the manner in which they do so. A study of development may also be expected to throw some light on certain other debatable points in the construction of the non-cellular tissues of the eye, and the

Digitized by Illinois College of Optometry Library

problem of the vitreous includes such questions as the origin of the fibres of the suspensory ligament of the lens, and the existence of a hyaloid membrane.

In the past the main controversies and investigations have concerned the following points:

1. The origin of the vitreous fibrils themselves.
2. The presence or absence of a membrane (hyaloid membrane) separating the vitreous posteriorly from the retina and anteriorly from the zonule and the back of the lens.
3. The origin of the fibres of the suspensory ligament of the lens and their mode of attachment to the ciliary epithelium on the one hand and to the lens capsule on the other.
4. The nature of the hyaline capsule of the lens.

The first point is the principal one, and a résumé of past work on the subject will be given. The other points will be discussed in describing the actual specimens, but, before enumerating the chief views which have been put forward, it may be useful to consider the question in a purely theoretical manner in the light of facts which have already been described.

In view of the development of the lens and optic cup it is obvious that there are only three types of cell in the neighbourhood from which the vitreous could be formed. These are:

1. Cells of the surface ectoderm which forms the lens plate.
2. Cells of the neural ectoderm of the primary optic vesicle.
3. Mesodermal cells lying between the two.

In considering a possible lental origin for the vitreous it is obvious that the lens must cease to function in this respect as soon as its hyaline capsule is complete, which, as we have seen, is at the 13 mm. stage. At this time the eye is exceedingly small and a great increase in the vitreous will be required to fill it in its final state. Since the vitreous is practically acellular it cannot increase in size *per se*, and it therefore seems unlikely that the lens alone can be responsible for the formation of it. On the other hand, the retinal layer of the optic cup, though it possibly remains undifferentiated slightly longer, also becomes bounded by a membrane, the internal limiting membrane, which would possibly seem to preclude any further rôle in vitreous production in regions where it is present. It is, however, true that an internal limiting membrane is not developed right up to the periphery of the inner layer of the optic cup after the 3rd month, so that the *pars caeca* may carry on the function of vitreous formation until development is complete. It must also be conceded that the internal limiting membrane, being cellular in nature and not a

Digitized by Illinois College of Optometry Library

structureless secretion product, is not entirely comparable with the hyaline capsule of the lens, and so does not necessarily denote by its presence a loss of continuity between retina and vitreous. It will be seen therefore that the possible part played by the retina is open to much discussion.

There remains for contemplation the mesoderm, and against a mesodermal origin of the vitreous is the contention that no mesoderm is at first present between the retinal surface of the optic vesicle and the lens plate, and that a vitreous space is recognisable before vascular mesoderm has grown into the optic cup. Furthermore, in large classes of vertebrates (birds, reptiles and amphibians) the amount of mesoderm entering the eye is extremely small and very transient, while the vitreous is extremely large. It seems therefore quite impossible on *a priori* grounds to postulate any single set of cells as origin for the vitreous. One is forced to compromise and admit the possibility of a three-fold origin, possibly simultaneous but probably successive, and it is with the exact part played by each component that modern investigation has mainly occupied itself.

Historical aspect of the problem. In 1848 Schöler (who was later supported by Virchow and Kölliker) stated that the vitreous was entirely mesodermal in origin, and that it could be looked on as a peculiar specialised form of connective tissue. This mesodermal theory of origin was unchallenged for nearly fifty years and was supported and taught by ophthalmologists and anatomists without question. Occasionally modifications and elaborations of the theory were put forward, and a certain amount of discussion took place as to whether, as originally stated, the mesoderm was present *in sitû* from the first as a thin lamina between the neural ectoderm of the optic pit and the surface ectoderm at the site of the future lens thickening, or whether it grew in secondarily through the foetal fissure, or whether, as Kessler suggested, the vitreous was in reality a sort of transudate from embryonic blood vessels in the interior of the eye. At any rate the main point, the entirely mesodermal origin, remained unchallenged.

In 1897, however, Tornatola published an account of the development of the vitreous which differed entirely from the accepted views. He based his conclusions on the examination of the embryos of a large number of mammals, including man (all in an extremely good state of preservation), and on a comparison of his results with the work of invertebrate embryologists such as Kleinenberg and Grenacher. He pointed out that the mesodermal theory was insufficient to account

Digitized by Illinois College of Optometry Library

for the facts, since in most animals the vitreous continued to develop after closure of the foetal cleft had severed connection with the surrounding mesoderm and also after the foetal intra-ocular blood vessels had atrophied. He therefore considered that the vitreous was ectodermal in origin and probably came from the retinal layer of the optic cup. It had already been shewn that in developing Annelids, Gastropods, Cephalopods, and other invertebrates the cells of the retinal layer are of two sorts, i.e. visual cells, which develop into the neurones concerned directly with appreciation of light, and secretory cells, the function of which is glandular, the "vitreous" of these animals being the product of their activity. In Gastropods the lens also is secreted by these glandular retinal cells. There seemed nothing improbable in this since, even in invertebrates, the retinal layers are ectodermal and it is from ectoderm that secreting organs are so often developed. The vitreous, in man, Tornatola therefore considered as an ectodermal secretion containing mesodermal cells which migrated into it but which were not in any way necessary to its formation. But the mesodermal theory of origin of the vitreous had held the field for so long that this paper passed almost unnoticed until a year after its publication, when Rabl, who was undertaking a detailed investigation of the development of the vertebrate lens, arrived at the same conclusion by independent observations.

From then onwards until the present day the ectodermal theory has been gaining ground, though opinions still differ as to the respective parts taken by the retina and the lens in the process and as to whether the mesoderm of the intra-ocular vessels is at all involved or not.

In 1902 v. Lenhossek described cone-shaped projections from the deep surface of the lens plate from which arose branching fibrils. They arranged themselves in radial and concentric sets: the radial fibrils reached the retina and gained attachment to its surface, the concentric ones formed a "capsula perilenticularis" or "anterior limiting membrane of the vitreous." These fibrils formed the basis of the vitreous, which was therefore primarily a product of lental (surface) ectoderm.

Thus we see that, though the originators of the ectodermal theory found the retinal (neural) ectoderm to be the source of the vitreous, later observers considered that the lens was responsible. It remained for a host of more recent workers to attempt to unify these conflicting views by describing, in very early stages, adhesions between optic vesicle and lens plate[1], which, stretching as the two separate,

[1] That no mesoderm was invaginated into the optic cup by the lens had been shewn by Kessler in 1875.

Digitized by Illinois College of Optometry Library

give rise to the appearance (on both lens and retina) of protoplasmic cone-shaped projections from which come fibrils, the intricate net-like union of which forms the vitreous. Speciale-Cirincione in 1903 advanced this view and it has also been ably supported by von Szily, Wolfrum, van Pee and others since. The vitreous so formed is present before any vascular mesoderm has grown in between the two ectodermal surfaces and is often alluded to as the "primary vitreous."

A "secondary vitreous," according to Cirincione, is developed later (after formation of the hyaline capsule of the lens) and contains a mesodermal element derived from the arteria hyaloidea and an ectodermal element from the retina in the region of the pars caeca. Certain of the fibres of this ectodermal element become coarser and form the fibres of the zonule, which is thus derived from neural ectoderm only, a fact which was admitted by v. Lenhossek, even though he denied any retinal component in the vitreous proper.

Druault (1904), however, gives yet another account of the process. The primary vitreous he describes as mesodermal, connected with the ingrowing vessels. As the eye enlarges, however, he considers that an outgrowth of "secondary" vitreous occurs from the retinal surface (ectoderm) and displaces the original mesodermal vitreous towards the centre of the eye. In this way is formed the appearance known as Cloquet's canal, which, according to Druault, is not a canal at all, but the primary mesodermal vitreous body displaced into the axis of the eye by the secondary outgrowth of vitreous from the retina. This primary vitreous finally disappears entirely, the definitive vitreous being therefore derived from neural ectoderm (inner layer of optic cup) only. This theory of the mesodermal origin of the primary vitreous does not enjoy very wide support, most observers tending to uphold the views put forward by v. Szily and others and summarised by Wolfrum in 1906.

There are thus three chief schools.

The earliest, and now the smallest, upholds the theory of the mesodermal origin.

The second states that the vitreous is ectodermal, some of the exponents considering it retinal (Tornatola), others lental (v. Lenhossek), and others (Cirincione) compounded of both.

The third and most popular at the present time (Wolfrum, Froriep, v. Szily) considers that all three types of cell (neural ectoderm, surface ectoderm and mesoderm) take part in the process, at different times and to a varying extent in different kinds of animals.

Tornatola first, and other observers since, have emphasised the important fact that all material used must be quite fresh, since the

Digitized by Illinois College of Optometry Library

fibrillar structure of the vitreous seen in embryos fixed while still alive soon gives place to a granular appearance if fixation is delayed[1].

According to Wolfrum, the first formed or primary vitreous is the result of the original adhesion between the neural and the surface ectoderm in the region of the lens plate. As these two surfaces separate, protoplasmic processes are pulled out between them, and an intermediate substance is formed by interlacing fibrils from this source. V. Szily has pointed out that such adhesions between epithelial surfaces and also between ectoderm and mesoderm are the rule rather than the exception throughout the body of the embryo in early stages. They form a non-cellular fibrous connective tissue uniting the basal cells of all epithelial surfaces, no matter from which germ layer, and are comparable to greatly attenuated inter-cellular protoplasmic bridges, such as have been described by Ranvier and other physiologists in adult tissue. In this way direct continuity becomes established between processes of mesodermal cells and fibrils derived from ectoderm, so that embryonic connective tissue anywhere may be looked on as containing always two components, the ectodermal one becoming in most situations unrecognisable at an early stage. In the region of the lens plate, however, there is no intervening mesoderm at first and the fibrils can be easily seen. They remain in continuity with both lens and retina until the separation of the lens vesicle and the formation of its hyaline capsule, which cuts them off from the lens. They remain thereafter in apposition to it, and form the *capsula perilenticularis*. After this stage they increase from the retinal side only, and the enlarging cavity of the optic cup is filled by them and also by mesoderm growing in through the foetal fissure, the stellate cells of which send out processes which join up in continuity with these ectodermal fibrils (in the same way that embryonic mesoderm becomes continuous with ectoderm elsewhere). The amount of mesoderm which enters the vitreous in this way varies extremely in different animals, being much greater in mammals than in any other species. As growth continues, these united fibrils become arranged in a regular manner parallel to the inner layer of the retina. This regularly arranged part is the beginning of the secondary or definitive vitreous. It appears in the region where the membrana limitans interna retinae is forming, and the outermost fibrils remain in permanent continuity with the glial cells of the retina (i.e. the foot-plates of the fibres of Müller). In the more anterior portion of

[1] It appears fairly certain from observations with the slit-lamp that a fibrous or membranous rather than a granular appearance is the most consonant with the condition of the vitreous in the living eye.

Digitized by Illinois College of Optometry Library

the retina the arrangement of fibrils parallel to the surface gives place to a radial arrangement, the fibrils arising from the summit of protoplasmic cone-shaped projections from the retinal surface exactly similar to those found at the posterior pole at an earlier stage. The latest formed of these fibrils become very stout and form the suspensory ligament of the lens, gaining a secondary attachment to the hyaline capsule of the lens. The mesodermal cells and blood vessels, which at one time formed so intimate a part of the vitreous, atrophy before birth, and the definitive vitreous can be looked on as mainly composed of ectodermal fibrils, which, however, unite to a certain extent with a few atrophic mesodermal remnants. Such, in general terms, is the most widely accepted view at the present day. Quite recently attempts have been made to revive the original mesodermal theory, but with scant success.

The Development of the Vitreous and the Suspensory Ligament of the Lens

This process, as it can be seen in well-preserved human embryos, will now be followed, and it should again be pointed out that the main differences of opinion to-day depend on the interpretation of the appearances seen, rather than on the actual existence of these appearances, which can be held to be generally admitted.

The development of the vitreous in the human embryo can be divided roughly into three periods of varying length, correlated with the part played by the different constituents.

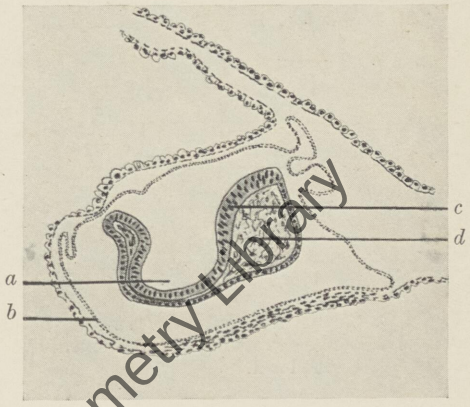


Fig. 128. Section through one optic pit of an early guinea-pig embryo. *a*, floor of optic pit; *b*, amnion; *c*, neural ectoderm; *d*, mesoderm.

First period of vitreous development (up to 13 mm. stage). The condition of the narrow interval between the outer face of the optic vesicle and the thickened patch of surface ectoderm forming the lens plate has already been described in dealing with the processes of growth of the lens. It will be remembered that no mesoderm intervenes between the two in the earliest stages and that there is definite continuity of protoplasm by fibrillar connections between the two. This continuity can probably, in man as in other vertebrates, be traced back without a break to the

Digitized by Illinois College of Optometry Library

earliest stage of formation of an optic pit on the floor of the wide open neural tube, and even possibly to earlier stages still, when the neural groove is first beginning to deepen. It is not confined to the region of the optic pit, but may be found all along the neural tube in the head region where the neural ectoderm is becoming continuous with the surface, but at varying times in different regions. Fig. 128 shews it in the region of the optic pit in a guinea-pig embryo.

Fig. 129 shews it in a chick embryo at the head end, but at a stage just before the optic pits have appeared. This continuity of proto-

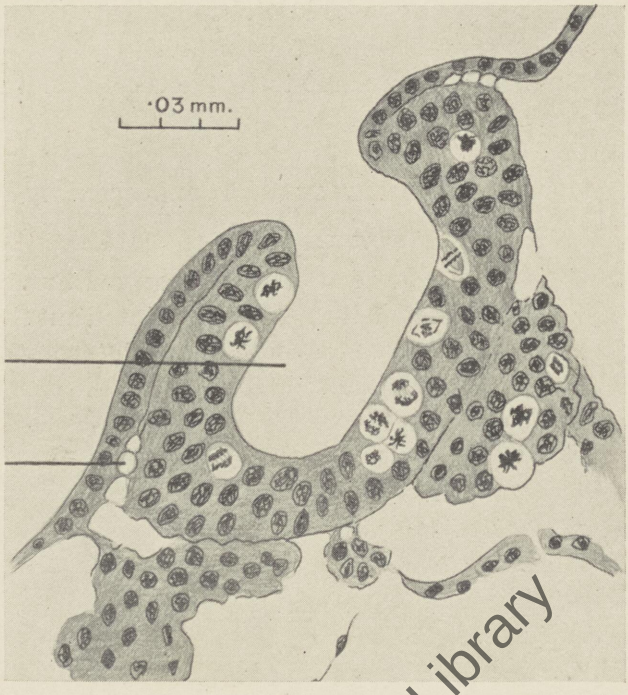


Fig. 129. Transverse section of anterior end of neural groove in an early chick embryo. *a*, neural groove deepening to form neural tube; *b*, protoplasmic continuity between neural and surface ectoderm.

plasm between neural and surface ectoderm is not therefore a phenomenon confined to one particular spot, and the region of the optic pit is merely peculiar in that it persists very much longer and can be seen very much more readily here than anywhere else in the embryo.

Fig. 130 shews where it can still be recognised at the 4·5 mm. stage, long after closure of the nerve tube and outgrowth of the primary optic vesicles. Fig. 131 shews the upper portion of the outer surface of the optic vesicle and the corresponding area of surface

Digitized by Illinois College of Optometry Library

ectoderm in contact with it. Even at this stage there are traces of invasion of the space by mesoderm, and in the figure five cells can be seen lying between the two ectodermal surfaces. These cells are derived from the mesoderm in contact with the lower surface of the optic vesicle, and represent the advance guard of those vaso-formative cells which will grow in through the foetal fissure to form the hyaloid

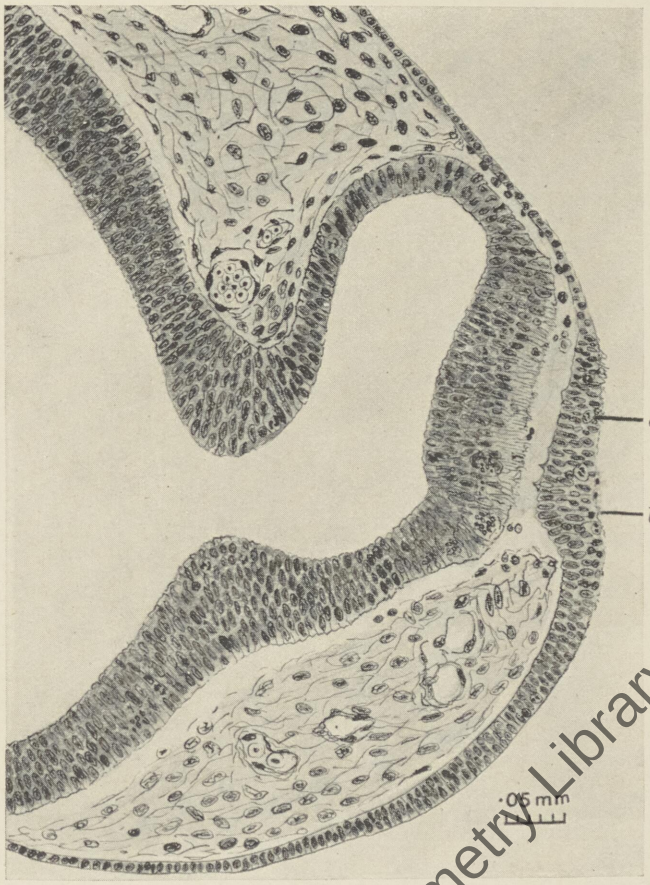


Fig. 130. Section through the lens plate and primary optic vesicle of a 4·5 mm. human embryo. *a*, cell in lens thickening undergoing mitosis; *b*, fovea lentis.

blood system at a slightly later stage. It will be seen that not only are the two ectodermal surfaces connected by fibrils but also the mesodermal cells have processes which become directly continuous with these fibrils, so that no distinct separation between the two germ layers can be seen. This fusion of mesoderm and ectoderm is of constant occurrence throughout the embryo at an early stage. It can be seen in Fig. 129, and involves both neural and surface ecto-

Digitized by Illinois College of Optometry Library

derm. In the 4·5 mm. human embryo from which Fig. 131 was drawn it could be seen all over the surface of the central nervous system. The protoplasmic cone-shaped processes seen in the figure projecting from the surface of the optic vesicle merely shew that at this stage this latter participates in a condition common to the whole



Fig. 131. Section through the upper outer part of the wall of the optic vesicle and adjacent ectoderm of a 4·5 mm. human embryo. *a*, surface ectoderm; *b*, cavity of optic vesicle.

of the central nervous system just as we have already seen that it participates in the general vascularisation[1].

In Fig. 132 the area of adhesion is much more marked and the cone-shaped processes larger. There is not in this or the preceding

[1] Seefelder, in describing the cells forming the walls of these retinal capillaries, considered them ectodermal. He thought that they were extruded from the retina and formed the vitreous as a product of their disintegration. From a closer study of their origin, however, it has been seen that they are mesodermal and play no part in the genesis of the vitreous at this stage.

Digitized by Illinois College of Optometry Library



Fig. 132. Section through the optic cup and lens pit of a human embryo of 5 mm.

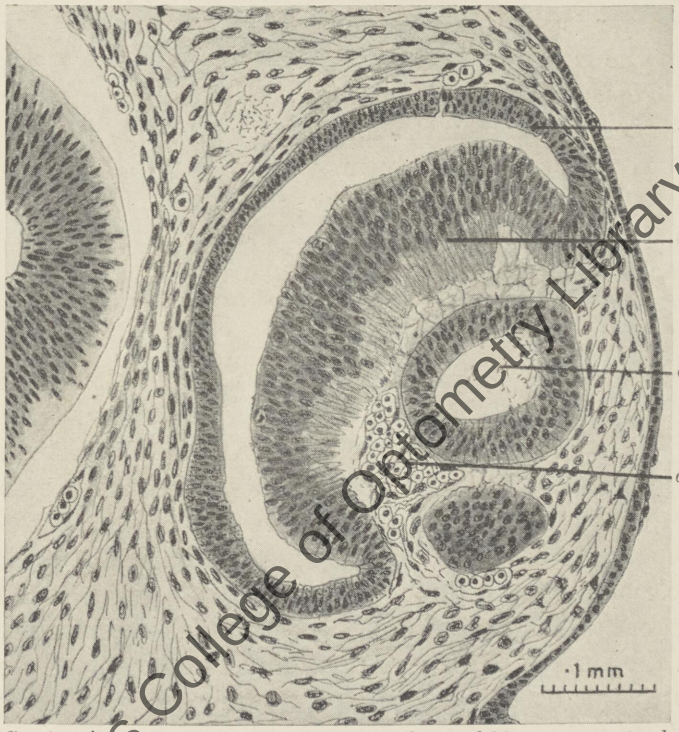


Fig. 133. Section through the eye of a human embryo of 10 mm. *a*, outer layer of optic cup; *b*, inner layer of optic cup; *c*, lens vesicle; *d*, blood vessel.

Digitized by Illinois College of Optometry Library

stage any doubt that both the retinal and the lental surfaces are involved equally in the production of these fibrils, which are not confined to any particular region, though they are most marked in the interior of the fast deepening optic cup. By 10 mm. (Fig. 133) the condition of things is beginning to be much modified by the ingrowth of large quantities of vascular mesoderm, so that the space between the now separated lens vesicle and the retina is occupied by a thin-walled blood vessel projecting into the eye through the foetal fissure. This invasion of the optic cup by vascular mesoderm appears to occur in all classes of vertebrates, but reaches its highest development in the mammal.

Fig. 134 shews how meagre in quantity it is in bird embryos and therefore how in these the lens and retina appear to take a much greater part in vitreous formation than they do in man. Fig. 135 shews the eye of an older chick embryo. It will be seen that no vasa hyaloidea propria are to be seen, nor is there any vascular capsule to the lens.

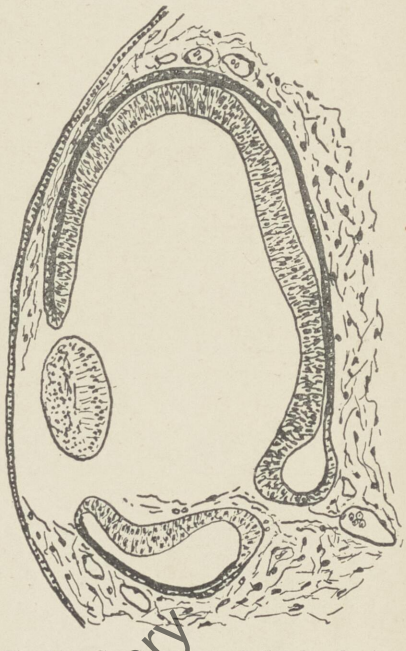


Fig. 134. Section through the developing eye of a 3½ days old chick embryo. The foetal fissure is seen at the lower part of the drawing with a small strand of mesoderm entering it.

The vitreous in birds is almost purely ectodermal. In man the entering blood vessel lies at first towards the lower part of the eye, and has few branches, so that at this stage (10 mm.) the original non-mesodermal fibrillar substance occupying the vitreous space can still be recognised in the upper part of the eye, where its continuity with lens vesicle and retina is still apparent. Even at this stage continuity of protoplasm can be found all over the embryo, and in the eye it exists not only between lens and retina, and between both and the vasoformative mesoderm, but also between the lens vesicle (now separated) and the surface ectoderm and intervening mesoderm. Fig. 136 shews the lens vesicle of a 12 mm. human embryo. The projections from its surface connecting it with retinal ectoderm, with vascular mesoderm, and with the surface (both mesoderm and ectoderm) can be clearly seen. Up to this age, then, we can definitely say that the vitreous space is filled with a mass of fibrils, derived from the lens and the

Digitized by Illinois College of Optometry Library

retina and joining up secondarily with fibrils from the cells of the wall of the hyaloid artery. This is the *primary vitreous*. It is originally purely ectodermal, but becomes intimately connected with mesoderm as soon as invagination of the optic vesicle begins. The first stage,

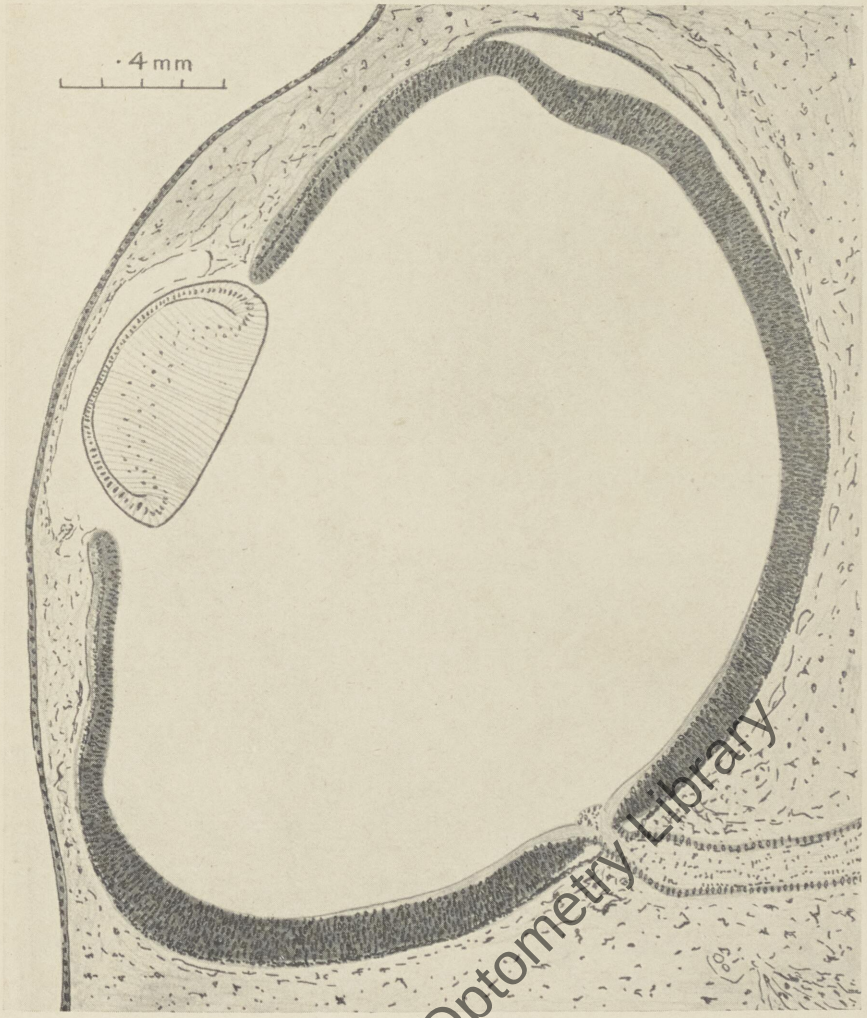


Fig. 135. Developing eye of chick after closure of the foetal fissure.

or stage of development of the primary vitreous, ends with the appearance (at 13 mm.) of the hyaline capsule of the lens. This can be seen in Fig. 137 (human lens from embryo of 13 mm.) and it is obvious that the lens can take no further part in vitreous formation after this, though vitreous fibrils remain adherent to the

Digitized by Illinois College of Optometry Library

capsule. These vitreous fibrils close to the lens condense somewhat, and can be recognised afterwards as a thin fibrous envelope surrounding the lens and containing in its meshes the vessels of the vascular

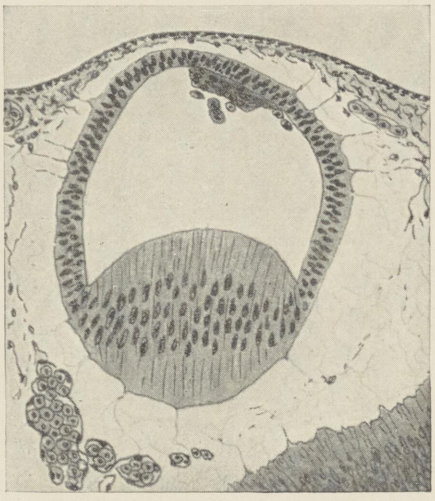


Fig. 136. Section through the lens vesicle of a human embryo of 12 mm.

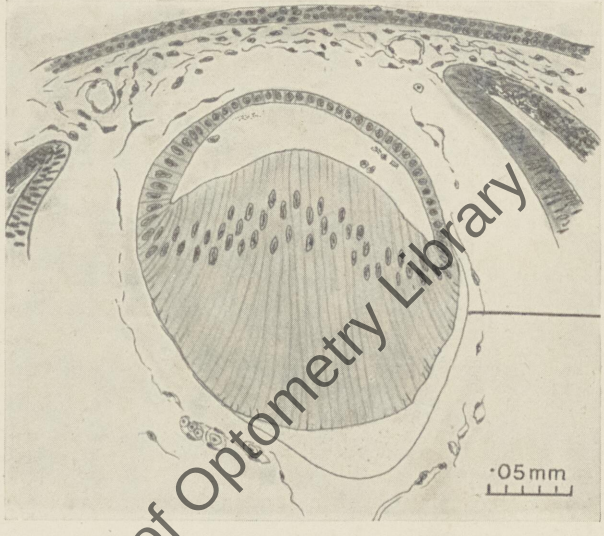


Fig. 137. The lens of a 13 mm. human embryo. Note the appearance of the hyaline capsule *H*.

capsule. This fibrous capsule can be called the *capsula perilenticularis fibrosa*. It is derived from the lental part of the primary vitreous and serves to mark the final situation of this.

Digitized by Illinois College of Optometry Library

The second period of vitreous development (13–65 mm.) begins at the 13 mm. stage. The whole of the retinal surface remains in continuity with the vitreous, but a definite line of separation begins to be recognisable about this time at the posterior pole, where the fibres of Müller are reaching the surface and beginning to unite with each other to form the *membrana limitans interna*. The Müllerian fibres themselves appear to be continuous with the vitreous fibrils, and the

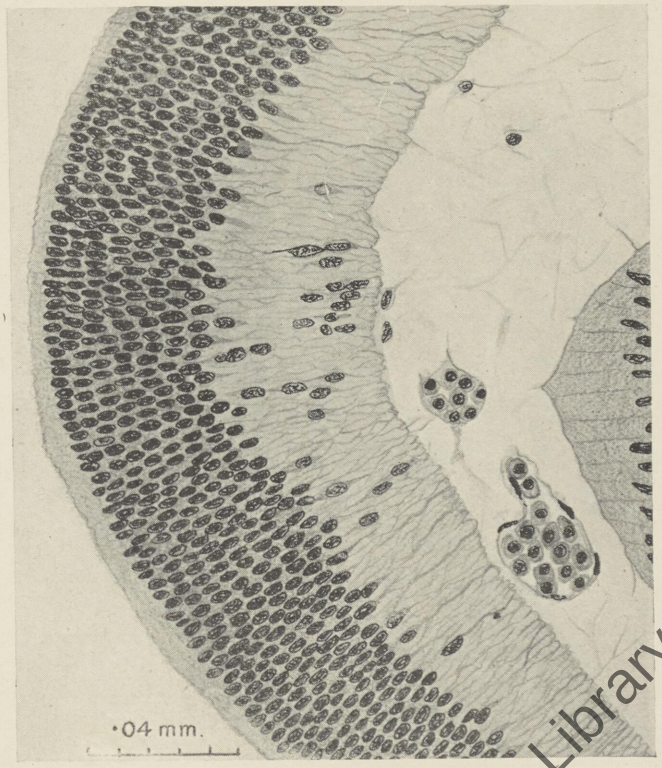


Fig. 138. Section through the inner layer of the optic cup of a 12 mm. human embryo.

internal limiting membrane is not in any sense a surface of separation. It is strongly united to the vitreous, and when shrinkage occurs from any cause the foot-plates of the Müllerian fibres tear away from their retinal attachments and remain in continuity with the vitreous. In view of this continuity it is possible that the presence of a differentiated membrana limitans interna does not necessarily preclude the retina from further formation of vitreous. Fig. 138 shews an early stage (12 mm.) of the membrana limitans interna. It appears first at the posterior pole. In the lower part of the eye it is delayed and Fig. 139 shews that there is here free union between retinal cells

Digitized by Illinois College of Optometry Library

and mesoderm cells around the entering hyaloid artery. In the upper portion of the eye the internal limiting membrane can soon be recognised right up to the margin of the cup. Fig. 140 shews a portion of the upper part of the margin of the cup of the same embryo. The fibres of Müller and their foot-plates and the membrane formed by their union can be clearly seen, as also can the extremely intimate connection of this latter with the vitreous. At the margin the internal limiting membrane has become detached during fixation and a space appears between it and the retina. It may be noted in passing that the same thing may happen in the adult as a result of injury during life, a sub-hyaloid haemorrhage being the result and the separation

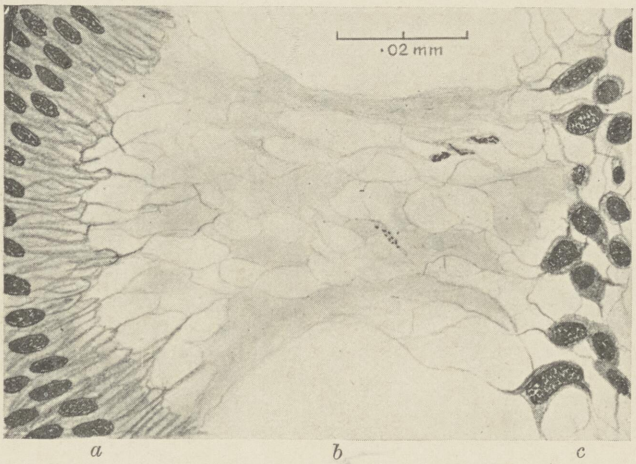


Fig. 139. Section through the inner surface of the retina and the adjacent vitreous at the lower part of the optic cup of a 12 mm. human embryo. *a*, retina; *b*, vitreous; *c*, mesoderm.

occurring in exactly the same plane. In this specimen it is quite apparent that no membrane other than the internal limiting membrane separates retina from vitreous and that this membrane is most intimately connected with both. Observations on all later stages agree in this that there is never any definite evidence of the existence of a hyaloid membrane separating the internal limiting membrane from the vitreous. A hyaloid membrane in this situation, if it existed, might be taken to be a structureless membrane, possibly of a cuticular nature, secreted by cells and resembling in the main the hyaline lens capsule, but thinner. Such a membrane would definitely hinder the retina from taking any further part in the formation of fresh vitreous. The membrana limitans interna, on the other hand, is formed of definite protoplasmic processes of cells, and remains, through the inner limbs of the fibres of Müller, in connection with

Digitized by Illinois College of Optometry Library

the cell body and nucleus throughout life. There seems very little difficulty therefore in supposing that the foot-plates of the Müllerian fibres are themselves concerned in the production of vitreous fibrils during growth of the eye, since they are glial in nature and are intimately connected in their development with the marginal layer (also glial) of the wall of the optic vesicle, which obviously plays a large part in the production of the primary vitreous. It must not be forgotten that many observers look on the presence of an internal limiting membrane over a given area as a sign that that area of the retina has ceased to form vitreous. This is, however, hard to accept in view of the presence of a limiting membrane right to the margin

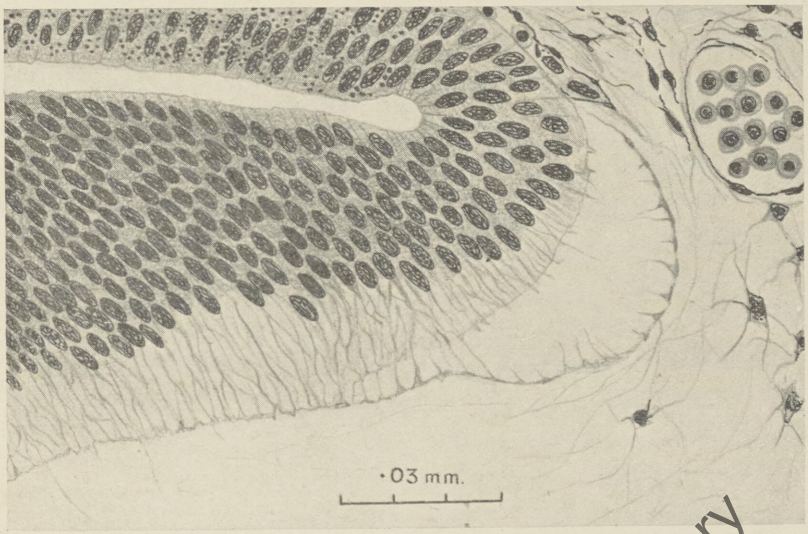


Fig. 140. Section through the margin of the optic cup of a 12 mm. human embryo.

of the cup from the 13 mm. stage to the 48 mm. during which period the eye and included vitreous continue to enlarge.

The eye continues to enlarge, and the hyaloid vessel gives off a complicated system of branches, some of which ramify in the vitreous (*vasa hyaloidea propria*) while others form a close network (*tunica vasculosa lentis*) on the surface of the hyaline lens capsule and in the layer of primary vitreous represented by the capsula perilenticularis, and anastomose around the equator of the lens with vessels in the mesoderm outside the optic cup. At 26 mm. these two sets of vessels can be seen (Fig. 141). The cells composing their walls are in continuity with vitreous fibrils which in turn are still adherent to the retina, though foot-plates of Müllerian fibres are in contact all over the surface.

Digitized by Illinois College of Optometry Library

Fig. 142 shews a portion of the vitreous seen under a high power (from an embryo of 25 mm., slightly younger than that seen in Fig. 141). The edge of the retina is seen, and the continuity of the

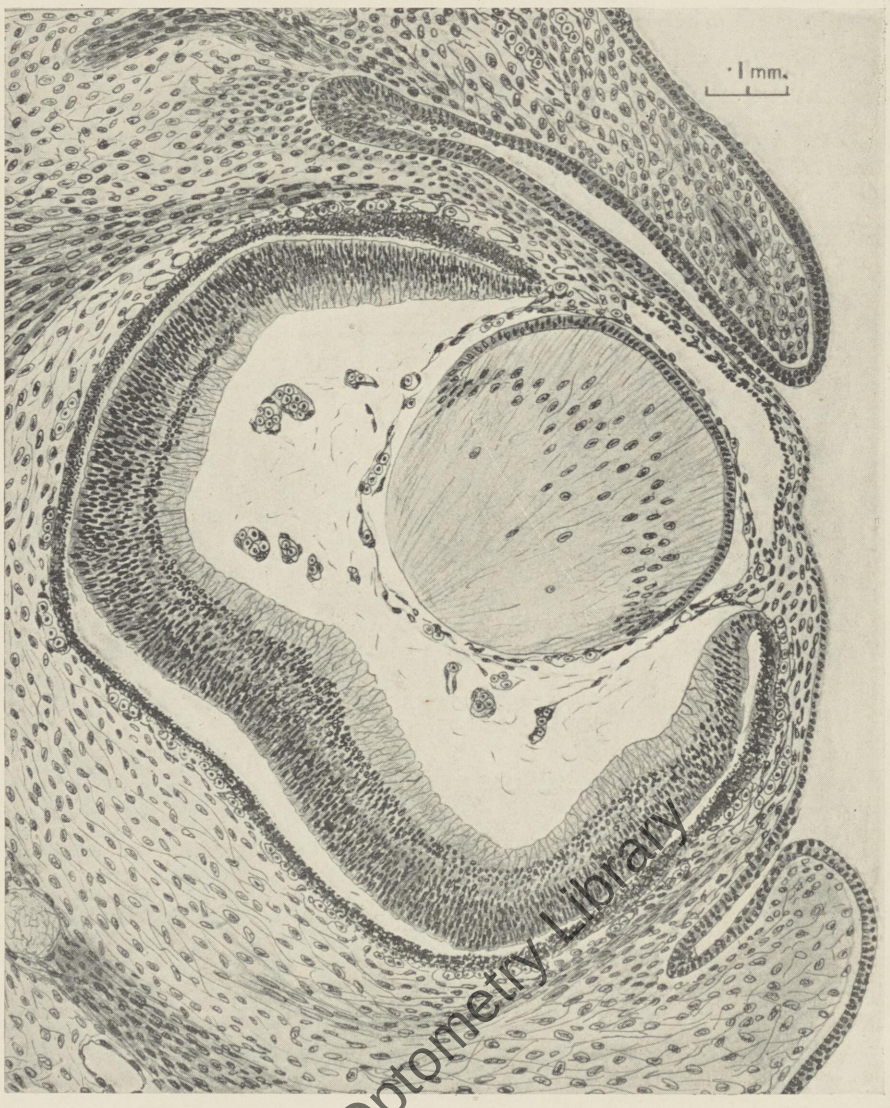


Fig. 141. Section through the eye of a 26 mm. human embryo. Note the vasa hyaloidea propria in the vitreous and the vessels in contact with the lens capsule and around the opening of the cup.

Müllerian fibres with the vitreous fibrils and with the internal limiting membrane is obvious in the lower part of the drawing. About the centre are seen two isolated stellate mesoderm cells derived from the walls of the vasa hyaloidea propria, and the richly anastomosing

Digitized by Illinois College of Optometry Library

processes which link them up with the surrounding fibrillar net of the vitreous are quite obvious. In the upper part can be seen one of the vasa hyaloidea propria, its walls shewing a similar continuity of protoplasm. From this drawing is apparent the utter impossibility of postulating of any given vitreous fibril exactly how much of it is ectodermal and how much mesodermal. That at this stage in man

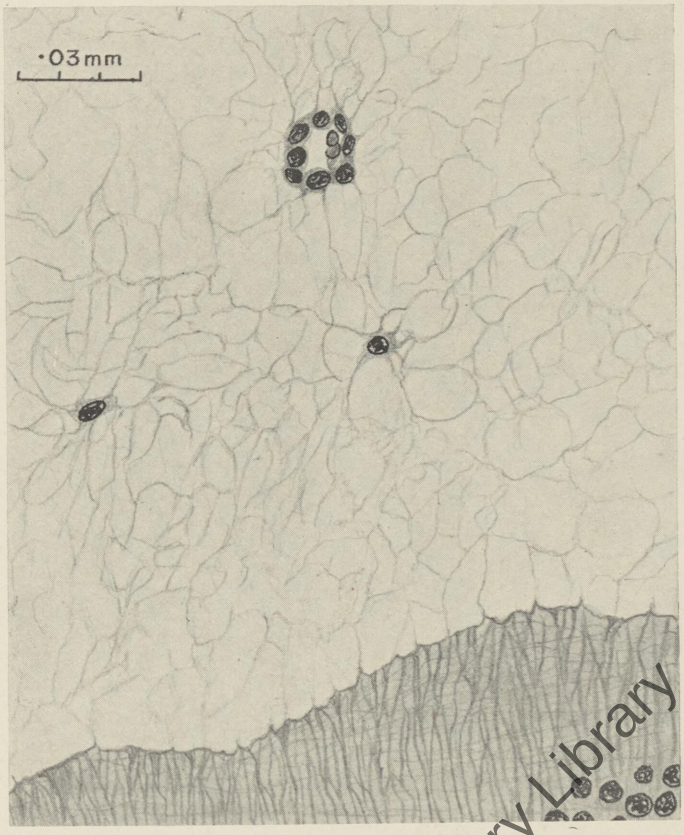


Fig. 142. The vitreous at the 25 mm. stage. Note the fibrillar network in continuity with the mesoderm of the vessels and the ectoderm of the retina below.

there is a mesodermal element is undoubted. This is richer in the region of the margin of the cup. Fig. 143 shews a high power view of the gap between the edge of the optic cup and the equator of the lens in the 26 mm. embryo seen in Fig. 141. All the cells in the gap are mesodermal, some forming walls of small blood vessels, others apparently being wandering stellate cells, like those seen in Fig. 142. There is a fibrillar continuity between all the cells and also between them and the surface of the internal limiting membrane, but the

Digitized by Illinois College of Optometry Library

hyaline capsule of the lens, though it is in contact with many of the mesoderm cells, does not seem to be in direct continuity with them or the fibrils. This state of affairs lasts until about the 40 mm. stage. Fig. 144 shews a section through the whole eye of a 35 mm. human embryo. It will be seen that the vitreous is still full of vessels right to the periphery, and the interior of the eye resembles that seen in



Fig. 143. Section shewing mesoderm between the margin of the optic cup and the lens in a 26 mm. human embryo. *M*, margin of optic cup; *L*, lens.

Fig. 141, with the possible exception that the tunica vasculosa is applied rather more closely to the lens.

Soon after this stage the smaller vessels in the vitreous begin to atrophy, the end nearest to the lens remaining visible the longest, with the result that the region of the vitreous near to the retina becomes free of vessels. When this happens the vitreous mesh becomes closer in the avascular region and there is a tendency for the fibrils to be arranged in a rather more orderly manner in two sets crossing one another, parallel to and at right angles to the surface

Digitized by Illinois College of Optometry Library

of the retina, those of the latter set being fewer. This avascular area has been named the *secondary vitreous* by many writers. Its appearance is due, in the first instance, to atrophy of the proximal ends of

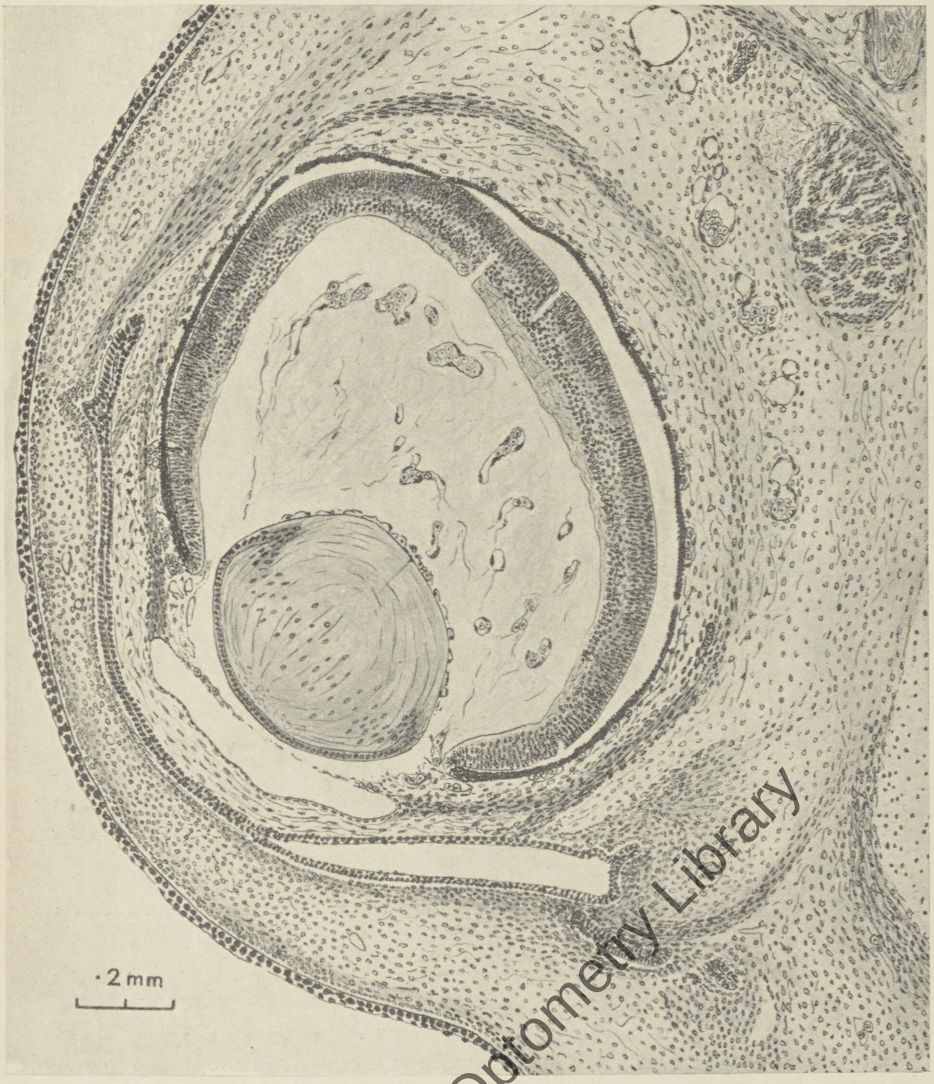


Fig. 144. Section through the eye and surrounding structures in a 35 mm. human embryo.

the vasa hyaloidea propria within it, but after this it is augmented by fresh vitreous formed from the retina as the eye enlarges, so that one gets the impression, in looking at successive stages, of a crowding together of the remaining vessels into the centre of the eye, and a compression of the primary (vascular) vitreous around them by the

Digitized by Illinois College of Optometry Library

denser secondary (avascular) vitreous[1]. Actual measurements, however, shew that no real compression takes place, and that the appearance is caused by a slowing and final cessation of growth of the primary vitreous containing the remaining vessels, together with a rapid increase in size of the whole eye. This naturally leads to a relative but not absolute decrease in the size of the primary vitreous. A glance at Fig. 145 will shew the lens and vitreous body of the eye of a 48 mm. human embryo in which this process of atrophy of the vasa hyaloidea propria is beginning. It can be seen that the mesh of the vitreous in the centre of the eye (in the region of the remaining

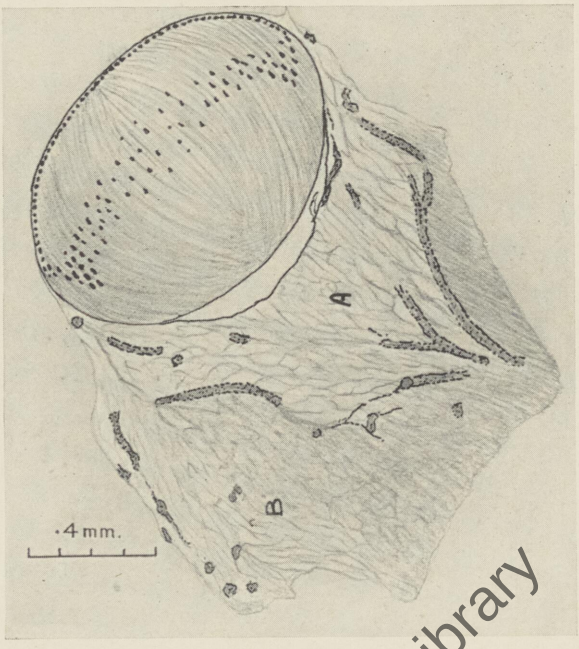


Fig. 145. The lens and vitreous of a 48 mm. embryo. *A*, primary vitreous; *B*, secondary vitreous being formed at this stage by disappearance of vasa hyaloidea propria.

vessels) is looser than that at the periphery, i.e. a distinction between primary and secondary vitreous is beginning. There is not much difference in size between the two at this stage. Also the looseness of the primary vitreous supports the idea that there is no pressure on it.

Fig. 146 shews a similar section through the eye of a 65 mm. human embryo. It will be seen that the avascular region is both

[1] It must be remembered that the secondary vitreous contains in its central portion some fibrils derived from the lens plate. It is not true to describe the secondary vitreous as derived entirely from the retina. It is actually at first all the avascular vitreous left by the atrophy of the vasa hyaloidea propria.

Digitized by Illinois College of Optometry Library

relatively and absolutely much larger than in the 48 mm. embryo but (both drawings being of the same magnification) an actual measurement will shew that the width of the primary vitreous, at its widest part just behind the lens, is unchanged, i.e. it has merely ceased to grow. Indeed its actual width here, approximately 1 mm.,

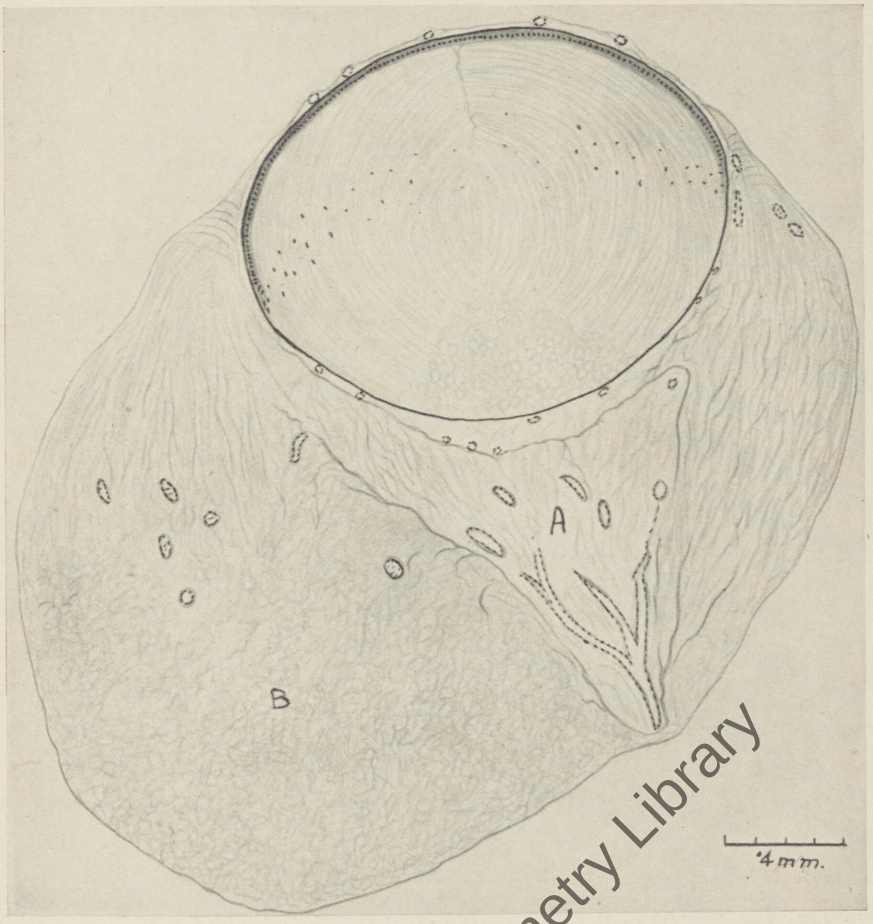


Fig. 146. Lens and vitreous of a 65 mm. human embryo. Magnification the same as in Fig. 145. *A*, primary vitreous; *B*, secondary vitreous increasing by addition from the retina

both at the 48 mm. stage and in later stages, corresponds quite well with the diameter of the so-called arc line, which is seen with the slit-lamp in the living adult and marks the area within which the terminal branches of the hyaloid reached the lens at the 3rd month, i.e. at the height of their development. Druault's contention that the region of Cloquet's canal represents the primary vitreous body compressed into the centre of the eye by the secondary vitreous

Digitized by Illinois College of Optometry Library

formed from the retina can therefore be considered suggestive, if one remembers that no actual compression takes place in it, but merely a cessation of growth. The main trunk of the hyaloid artery persists much longer than the vasa hyaloidea propria and increases in length *pari passû* with the growth of the whole eye, since it is adherent, on

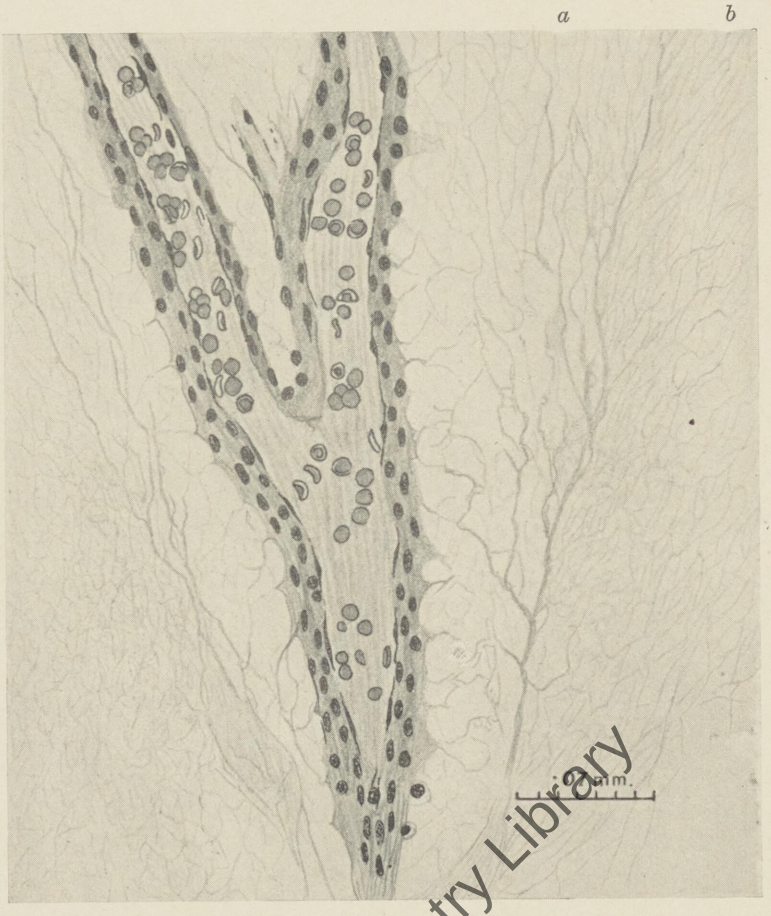


Fig. 147. Longitudinal section of Cloquet's canal and the contained hyaloid artery of a 65 mm. human embryo. The vessel, containing erythrocytes and lined by endothelium, is bifurcating. The condensation between primary and secondary vitreous is seen forming the wall of Cloquet's canal. *a*, primary; *b*, secondary vitreous.

the one hand, to the back of the lens, and on the other to the centre of the optic disc. The primary vitreous (derived from both lens plate and optic vesicle) adhering to it is of a looser mesh than the secondary (derived mainly but not entirely from the retina) and a distinct line of condensation of fibrils can be seen where they meet. This forms the so-called wall of Cloquet's canal. It is not a true wall but merely a line of meeting of a denser with a looser mesh in

Digitized by Illinois College of Optometry Library

the same network of fibrils. There is no evidence of a definite structureless hyaline membrane lining it. Fig. 147 shews it in longitudinal section at the point of division of the hyaloid artery (65 mm. stage). The vessel has a fairly wide bore. It contains red blood cells, of which by this stage a large proportion are no longer nucleated. The walls of the vessel are lined by a flattened endothelium and are composed, outside this, of two layers of undifferentiated mesodermal cells, the outer layer of which shews innumerable fine processes which unite with the fibrils of the primary vitreous. At some little distance from the vessel can be seen a line of condensation marked by thicker fibrils, outside which, again, the vitreous mesh (secondary vitreous) is less coarse and open than it is nearer the vessel. These thickened fibrils mark the boundary of the so-called canal of Cloquet in which the hyaloid artery runs. The intimate connection which exists between the wall of the hyaloid artery and the primary and the secondary vitreous here is apparent.

This channel of looser mesh running through the vitreous is funnel-shaped, narrow at its commencement on the disc and widening slightly towards its lental end, where it presents a circular open mouth applied to the lens, a little below and to the nasal side of the posterior pole. Within this open mouth of the funnel the hyaloid artery breaks up into many branches which ramify on the surface of the lens among the meshes of the capsula perilenticularis.

Fig. 148 shews some sections and an explanatory diagram of the canal of Cloquet in a 5 months foetus. The appearance of the ring of condensation forming the wall and its relation to the hyaloid artery are very similar to that seen in Fig. 147.

Fig. 149 shews the open lental end of the canal in a 110 mm. foetus, seen in transverse section. The section is very slightly oblique, so that a small portion of the lens with the branches of the hyaloid artery on it is seen within the circle, breaking its right hand edge. The original position of this circle or a portion of it can be seen on the posterior surface of the lens capsule even in the adult, and is known as the arc line (or Bogenlinie). It is very variable in shape and in the completeness and ease with which it can be seen, but it is practically always associated with a thin filament, the remains of the main trunk of the hyaloid artery, which hangs down from its centre. This circle or arc therefore represents the area on the lens within which the hyaloid artery breaks up into branches at the height of its development. It does not represent the final stage of the anterior end of Cloquet's canal.

At 65 mm. the surface of junction between primary and secondary

Digitized by Illinois College of Optometry Library

vitreous can be traced from the lental end of Cloquet's canal peripherally over the whole of the posterior surface of the lens. The lens lies directly embedded in primary vitreous (which contains the vessels

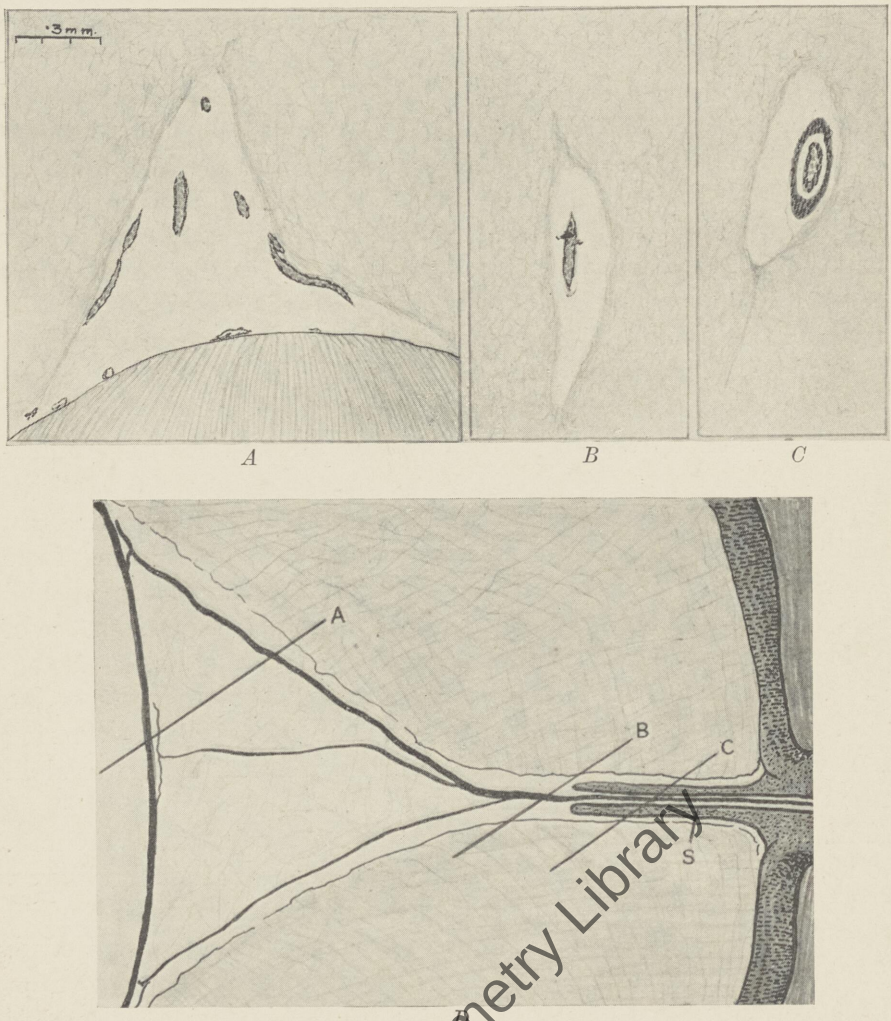


Fig. 148. *A*, *B* and *C*, sections across the canal of Cloquet in a 5 months foetus at the positions indicated by the lines in the reconstruction *D*. *A* shews the anterior funnel-shaped end of Cloquet's canal filled with loose-meshed primary vitreous, in which ramify the terminal branches of the arteria hyaloidea. *B* shews the canal containing the hyaloid artery near the centre of the vitreous. *C* shews Cloquet's canal containing the hyaloid artery enclosed in a glial sheath produced by the ectoderm of the optic disc. *D*, reconstruction shewing position of sections *A*, *B* and *C* and the glial sheath (*S*) of the hyaloid artery.

of the tunica vasculosa lentis) from which it is only separated by its own structureless capsule, to which vitreous fibrils and vessels are adherent. This layer of primary vitreous is very thin and contains

Digitized by Illinois College of Optometry Library

an irregular line of coarser and more condensed fibrils (the capsula perilenticularis) which separates it from the secondary vitreous. This condition is seen in Fig. 150, which shews the posterior surface of the

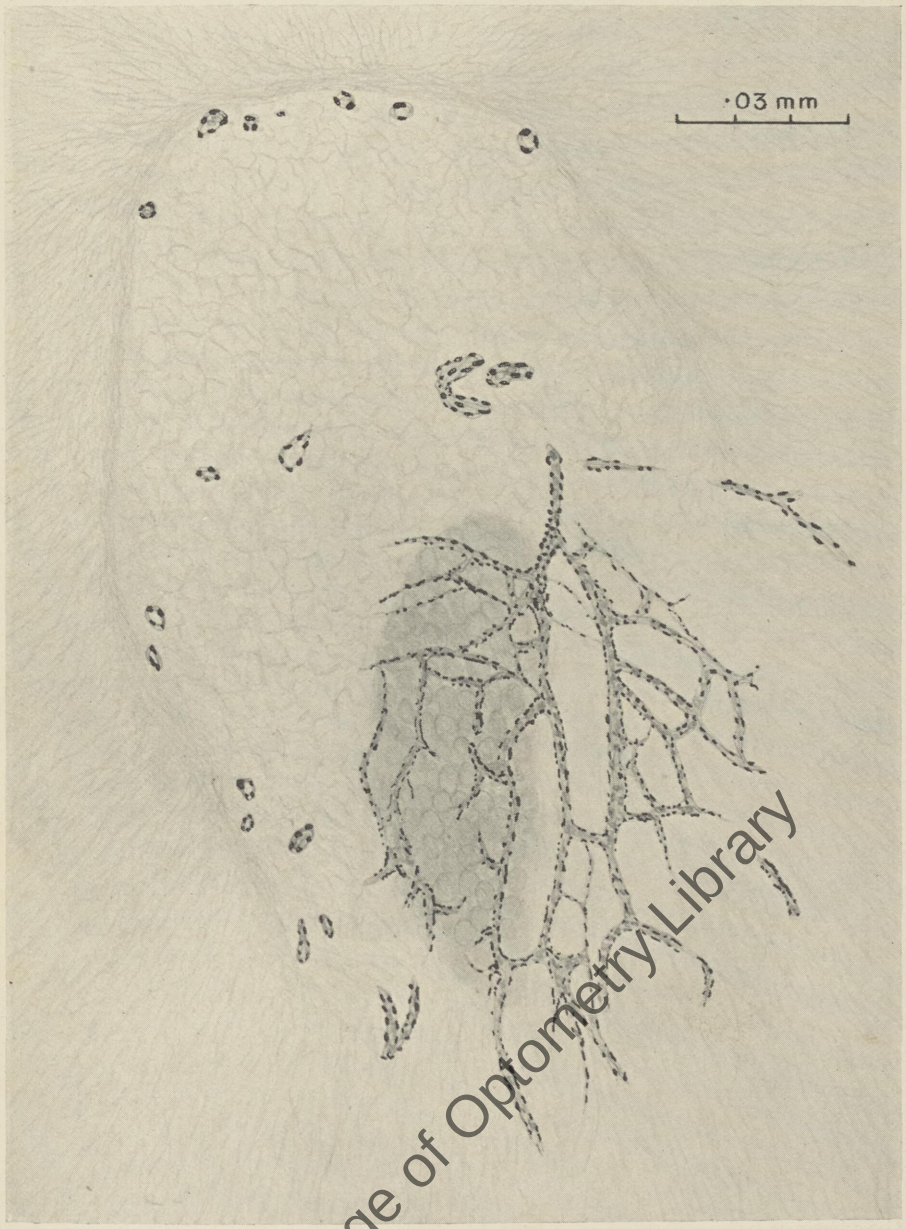


Fig. 149. Transverse section through the anterior end of Cloquet's canal in a 110 mm. human foetus. The ring of condensation forming the wall of the canal can be seen, and within it a portion of the lens covered by the vessels of the posterior vascular capsule. The contrast between the looser mesh of the vascular primary vitreous and the avascular secondary vitreous outside Cloquet's canal should be noted.

Digitized by Illinois College of Optometry Library

lens of the 65 mm. embryo. It will be seen that the vessels of the tunica vasculosa lentis are connected by fine fibrils which in turn are attached to an irregular line of coarser fibrils connected with the secondary vitreous behind. A few mesoderm cells and two capillaries are seen in this latter, shewing that it does not become entirely avascular until the complete atrophy of the vasa hyaloidea propria after this stage. This line of condensation between the vitreous of finer and the vitreous of coarser mesh is the "anterior portion of the hyaloid membrane" described by anatomists as lining the fossa patellaris of the adult vitreous, and the fibrous "capsula perilenticularis" of embryologists.

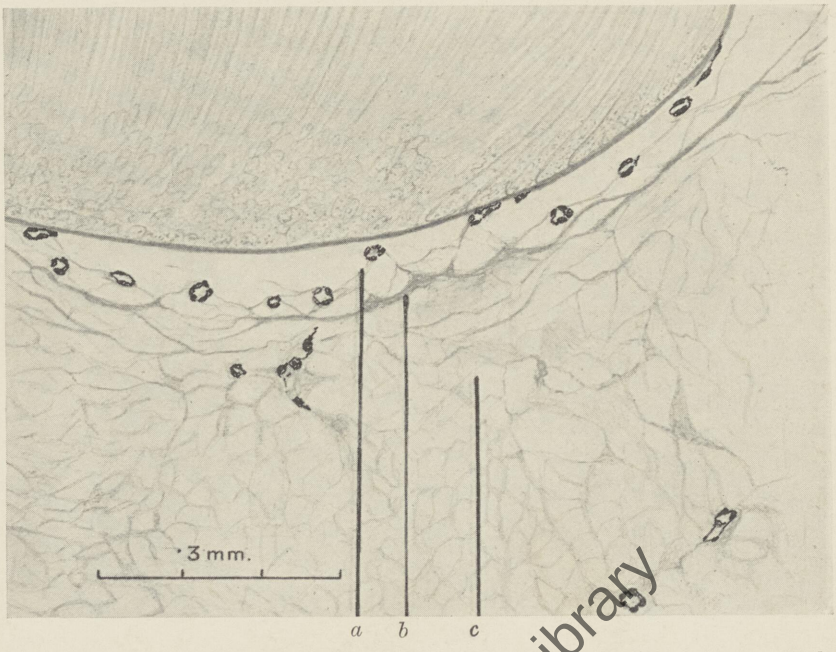


Fig. 150. Portion of the posterior surface of the lens in a 65 mm. human embryo. *a*, primary vitreous and vessels of the posterior vascular capsule of the lens; *b*, capsula perilenticularis or line of condensation in the primary vitreous separating it from the secondary vitreous; *c*, secondary vitreous.

Fig. 150 is especially interesting in view of the somewhat doubtful interpretation of the appearances seen in the living eye in this region. If a source of illumination, such as a Nernst or Nitra lamp, be employed in the slit-lamp, in most eyes a narrow interval will be seen between the back of the lens and the front face of the vitreous. This has been called the retro-lental space. All that can be seen in it are a few fine threads representing remains of the hyaloid artery and of the vessels of the tunica vasculosa lentis. The front of the vitreous behind it appears like a folded uneven curtain hanging down and waving with every movement of the eye. It has no smooth membrane covering it, and the amount of folding and the fibrillation of it vary very considerably in different individuals. It seems to have the same appearance as the rest of the vitreous behind, that is to say, a semi-membranous semi-fibrous structure,

Digitized by Illinois College of Optometry Library

unstable and allowing of movement within limits, in response to gravity, i.e. it is by no means solid. This front face of the vitreous, bounding the retro-lental space posteriorly, probably represents the old capsula perilenticularis, or line of condensation in the primary vitreous enclosing the vessels of the tunica vasculosa lentis, seen in Fig. 150. If a more brilliant source of illumination, e.g. an electric arc, be used in the slit-lamp, then, in proportion to the improvement in the illumination, so the retro-lental space will be seen to narrow and finally disappear, the region of it now being seen to be filled with fibrils like those in the rest of the vitreous, only much finer. This corresponds with the finer fibrillation and more open mesh seen in the primary vitreous within the capsula perilenticularis and within Cloquet's canal. The disputed hyaloid membrane is thus seen to be an area of condensation in the primary vitreous separating it from the secondary vitreous, not a membrane limiting the vitreous at all. This also is consonant with the fact that nothing approaching a hyaloid membrane is found in apposition to the internal limiting membrane of the retina.

At 65 mm. the capsula perilenticularis covers the whole of the posterior surface of the lens. It becomes more irregular in the region of the posterior pole, and fibres of it are reflected back along the main vessels and blend with the condensation of the wall of Cloquet's canal. It atrophies later completely in the region of the open end of the canal and at 5 months is continuous with the wall of this all round the funnel-shaped anterior mouth. These relations of Cloquet's canal and the so-called anterior portion of the hyaloid membrane remain practically unchanged throughout life, save for the almost complete disappearance of the blood vessels and for the atrophy and sagging down of the wall of Cloquet's canal mentioned below Further differentiation occurs in the antero-lateral regions after 65 mm.

Third period of development of the vitreous (65 mm. onwards). The relations of the developing vitreous to the equator of the lens must now be considered, and this brings us to the third period in its development; this begins about the 3rd month with the increasing growth rate of the margin of the cup. Up to this time the relations at the margin of the cup have been those seen in Fig. 143, in which mesoderm is passing round the edge of the cup and blending freely with the vitreous. As the eye grows, however, the mesoderm becomes more scanty and the direction of the fibrils of the vitreous more regular, until at 48 mm. the fibrils at the equator of the lens are all arranged more or less parallel to the surface of the optic cup here. This gives rise to the appearance described by Druault as the *faisceau isthmique* or *marginal bundle*. It can be seen in Fig. 151, and its surface represents the anterior limit of the secondary vitreous. It is to be noted that the internal limiting membrane of the retina

Digitized by Illinois College of Optometry Library

is co-extensive with the retinal surface of the secondary vitreous at this stage.

We have already seen that, from the 3rd month onwards, the margin of the optic cup grows actively and forms the ciliary region and the ectodermal layers of the iris. These newly formed portions of the optic cup resemble, in their character of a simple neuro-epithelium and in the possession of protoplasmic cone-shaped projections from their surface, the original ectodermal wall of the optic vesicle. Like it, they possess no internal limiting membrane, and, like it, they give

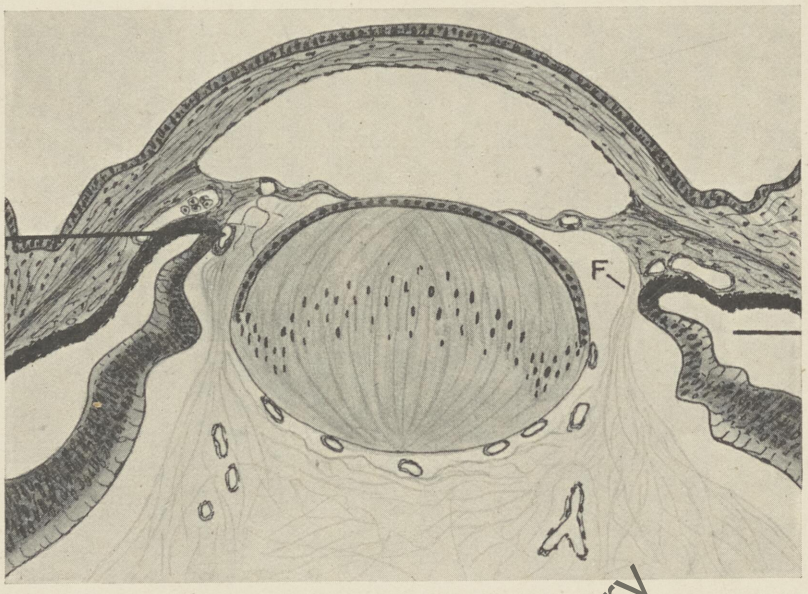


Fig. 151. Section through the anterior part of the eye of a 7·8 mm. human embryo. *A*, remains of cavity of primary optic vesicle; *F*, "faisceau isthmique" of vitreous; *G*, remains of capsulo-pupillary vessel.

rise to vitreous fibrils; these vitreous fibrils formed after the 3rd month from the growing margin of the cup may be called, for the sake of unity, the *tertiary vitreous*.

We have seen from Fig. 151 that the "faisceau isthmique" passes between the equator of the lens and the margin of the cup, to blend with the mesoderm in front of the eye. When, therefore, the outgrowth of tertiary vitreous fibrils begins here at the 3rd month, they run at first through this "faisceau," passing at right angles to its fibres (see Fig. 152). As they increase in number and in strength, for they soon become very coarse, they also become displaced further forwards by growth of the margin of the cup. The connection of the "faisceau isthmique" with the anterior mesoderm atrophies as

Digitized by Illinois College of Optometry Library

the iris grows and the ciliary folds develop, so that the "faisceau" merely retains its attachment to the retina at the ora serrata. The tertiary vitreous fibrils continue to develop in front of this attachment and a line of condensation on the surface of the secondary vitreous (continuous with the capsula perilenticularis) separates this finally from the tertiary or ciliary vitreous. Fig. 152 shews in a diagrammatic

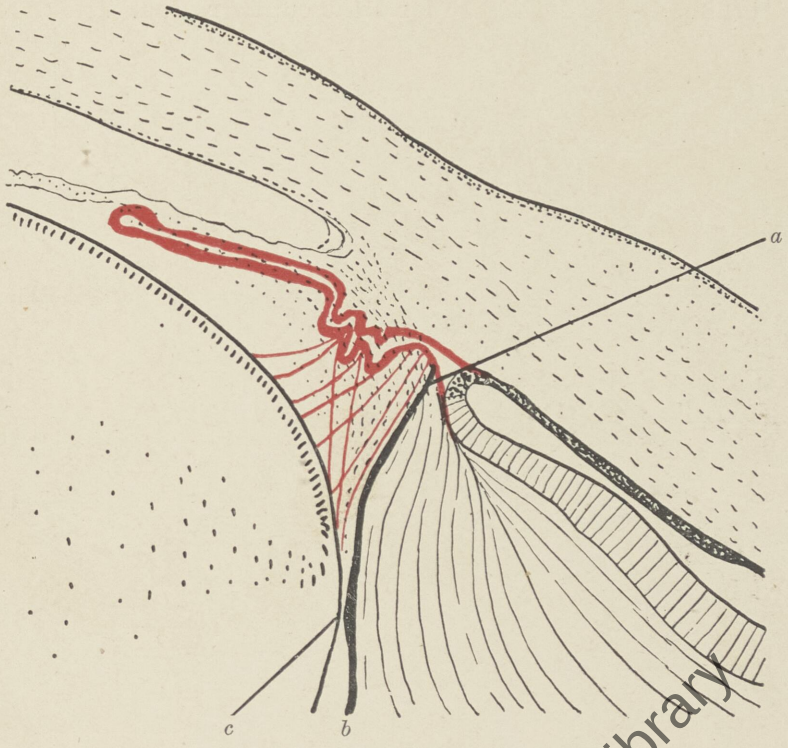


Fig. 152. Diagram illustrating the formation of the condensation between secondary and tertiary vitreous. The structures formed from the margin of the optic cup after the third month are shewn in red, as also are the fibres of the tertiary vitreous (zonule fibres). The "faisceau isthmique" is seen at *a*, the dotted portion atrophying with growth of the margin of the cup. The line at *b* represents the final surface of the secondary vitreous. *c* shews the point of adhesion between secondary vitreous and lens known as Egger's line.

manner how this line of condensation arises. At a point about 2 mm. from the equator of the lens this line of condensation becomes lightly adherent to the lens capsule. The ring so formed on the lens is known as Egger's line. Thereafter the fibrils from the ciliary region continue to grow and pass towards the equator of the lens. They gain attachment by adhesion to the surface of the hyaline capsule of the lens, the capsulo-pupillary vessels of the tunica vasculosa lentis having almost disappeared here. They finally become arranged

Digitized by Illinois College of Optometry Library

in a regular manner and form the fibres of the *suspensory ligament of the lens*. They can be recognised first at 65 mm. at which time they have barely reached the lens. They are well developed and shew the adult arrangement at 110 mm.

Fig. 153 shews a high power view of the ciliary region of a 65 mm. embryo. The edge of the lens is seen in the upper left-hand corner and the neuro-epithelium of the inner layer of the optic cup below. This is thinning and folding to form the ciliary region. The fibres of

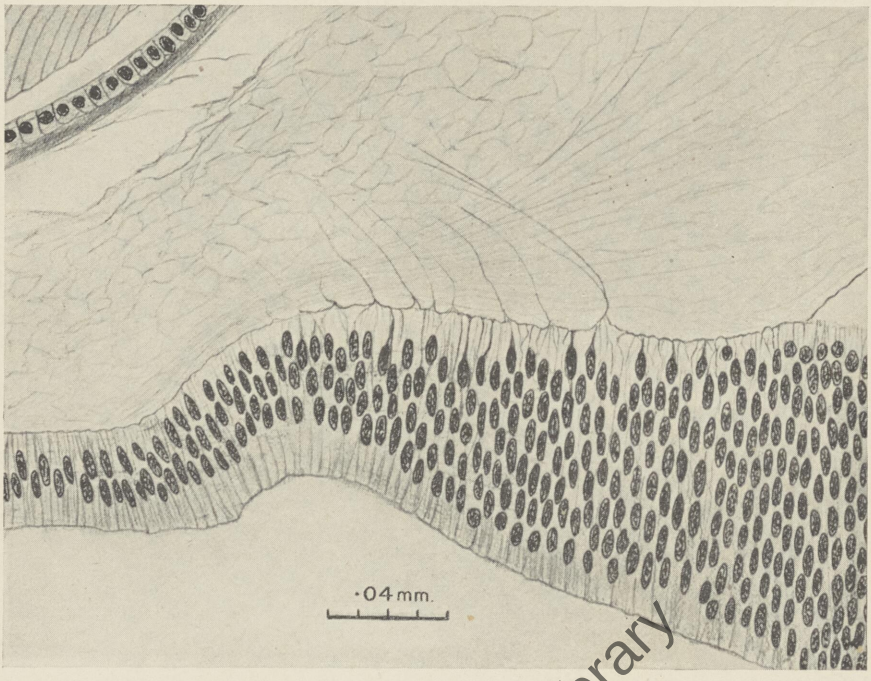


Fig. 153. Section shewing the developing suspensory ligament of the lens in a 65 mm. human embryo. Fibrils forming it are seen passing at right angles across the "faisceau isthmique" towards the lens. This portion of the "faisceau" will subsequently disappear. Cf. Fig. 152.

the "faisceau isthmique" are seen forming a condensed band lying along the surface of the ciliary epithelium and parallel with it. They fade away towards the lens into a looser mesh and have practically lost connection with the mesoderm outside the eye by this stage. The internal limiting membrane can be seen slightly detached at the right-hand end of the epithelium. Its point of attachment marks the position of the future ora serrata. The edge of the epithelium beyond this shews little points and projections, from the summits of which arise stout fibrils. These are the fibres of the tertiary vitreous. They cross the fibrils of the "faisceau isthmique" at right angles

Digitized by Illinois College of Optometry Library

and run towards the lens. Some of them shew a feeble attachment here. Others do not seem to have reached it yet.

With regard to the mode of attachment of the two ends of the fibres of the tertiary vitreous (or suspensory ligament of the lens, as it can now be called) there has been some controversy. At their ciliary ends they are obviously attached to the surface of the ectodermal cells themselves, since

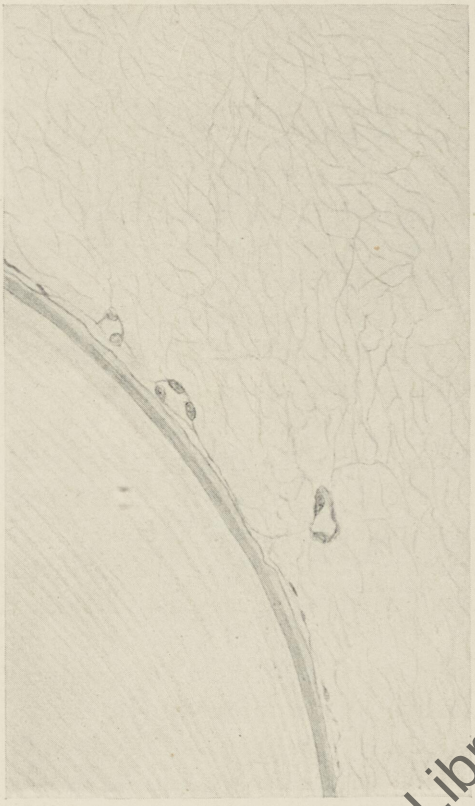


Fig. 154. Portion of the postero-lateral surface of the lens of a 5 months human embryo, shewing the atrophy of the vascular capsule and its distraction from the hyaline capsule of the lens. *V*, vascular capsule; *H*, hyaline capsule; *L*, lens.

they arise as processes of them. It has been suggested (Wolfrum) that in the adult they pass between the cells and gain attachment to a basement membrane or membrana limitans externa. This seems unlikely, both from their development and from the fact that in the adult there is no true membrana limitans externa in the ciliary region, since there are no Müllerian fibres to form it. At their lental ends they are firmly attached to what is known as the zonular lamella of the hyaline capsule of the lens. This, the outer portion of the capsule, has been considered by Schwalbe to be derived from mesoderm, but there seems very little ground for this assumption. It is not the remains of the vascular capsule, since this can be seen on the surface of the hyaline capsule, and its final complete atrophy and disappearance followed. Fig. 154 shews this in process of disappearance in a 5 months foetus. It might possibly

Digitized by Illinois College of Optometry Library

be formed by the coalescence of the ends of the zonule fibres themselves, but in that case it would probably not extend all round the lens. It is much more likely that the whole capsule, including the zonular lamella, is a secretory product of the lens itself.

After the 65 mm. stage the atrophy of the "faisceau isthmique" continues until its anterior limit coincides with the posterior limit of the tertiary vitreous or zonule fibres, to which it remains for some time firmly attached, i.e. at the future ora serrata. When this occurs a definite condensation takes place on the surface of the secondary vitreous, which condensation is in continuity laterally with the condensation in the primary vitreous behind the lens (capsula perilenticularis) and to which the name "anterior portion of the hyaloid membrane" is sometimes given. Laterally, therefore, this so-called hyaloid membrane separates the secondary vitreous from the tertiary or zonule fibres, and thus is seen everywhere to mark out the surface of the secondary vitreous, not to limit the entire vitreous body. Fig. 152 should again be considered, and the gradual regression of the secondary vitreous from the equatorial region of the lens noted.

Fig. 155 shews the process complete at term. The zonule fibres are perfectly distinct, and the line of condensation known as the hyaloid membrane can be traced behind them to the posterior boundary of the retro-lental space. This condition is present in the adult and it is obvious that many of the conflicting accounts of the anatomy of this region hang on the possibility of various interpretations of the word "membrane." If it is taken to mean a structureless and continuous single sheet of something applied to the face of the vitreous, then the hyaloid membrane can be said to have no existence either on the anterior or the posterior surfaces of the vitreous. If, on the other hand, it means a plane of discontinuity marked by a condensation of fibrils in the vitreous, then it does very definitely exist anteriorly, although it does not limit the vitreous in a developmental sense, but merely marks off the secondary vitreous from the primary and from the tertiary or zonule fibres. Posteriorly, according to either conception, it does not exist, there being at no time a membrane or condensation other than the internal limiting membrane separating the vitreous from the retina.

As the folds in the ciliary region become more marked they approach the lens and at 110 mm. are practically in contact with its equator all round. There is by this time complete atrophy of the "faisceau isthmique." The valleys between the processes are filled with zonule fibres arising directly from the summits of the cells. The apices of the folds, however, no longer give rise to any fibrils,

Digitized by Illinois College of Optometry Library

but have a smooth surface lying against the lens, which shews slight indentations to receive them. Thereafter the space between lens and ciliary body widens, and the fibres of the zonule become longer.

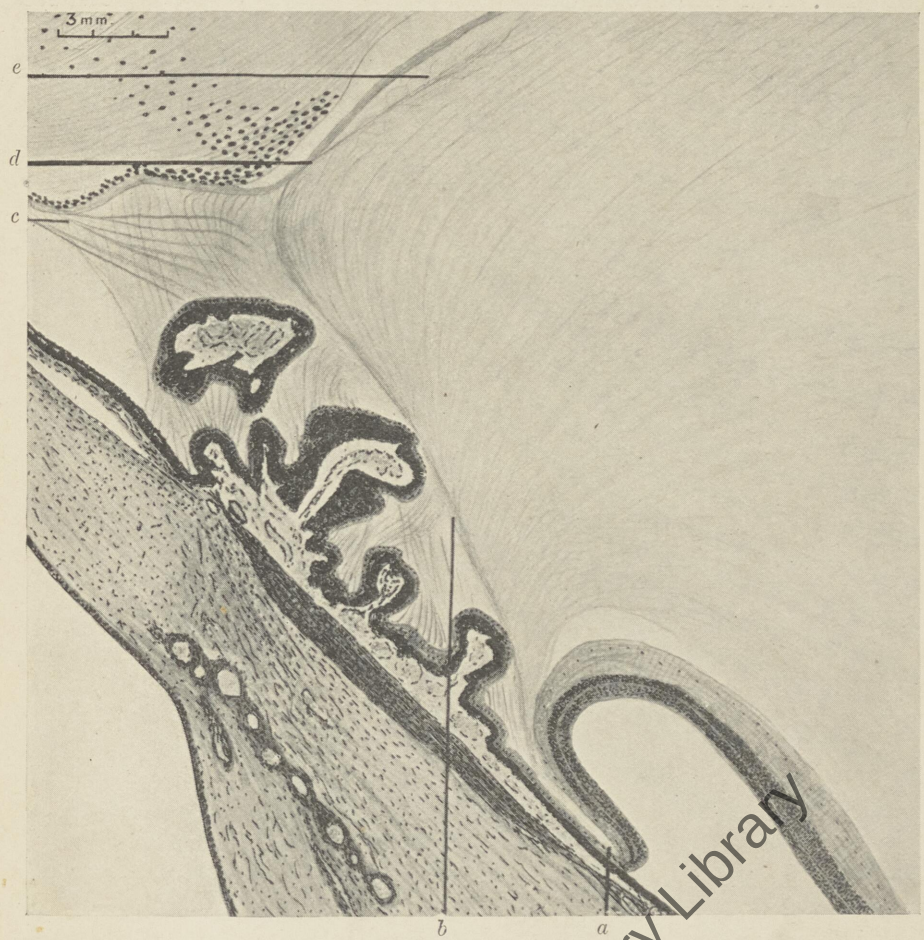


Fig. 155. Section through the ciliary region and adjacent vitreous of a foetus at term. *a*, ora serrata; *b*, condensation separating vitreous proper from zonule fibres (i.e. secondary from tertiary vitreous); *c*, zonule fibres attached to lens; *d*, Egger's line; *e*, retro-lental space.

Fig. 156 shews an equatorial section of the lens and ciliary body at the stage of great approximation. The three periods of vitreous development may be summarised thus:

1. **First period**, up to 13 mm. Formation of primary *vitreous* from ectoderm of lens plate and optic vesicle, with secondary ingrowth and incorporation of vascular mesoderm. This stage ends with the secretion of the hyaline capsule of the lens, which prevents the lens taking any further part in vitreous production.

Digitized by Illinois College of Optometry Library

2. **Second period**, up to 65 mm. Formation of *secondary vitreous* from fresh outgrowth from inner layer of optic cup, and from peripheral portion of existing vitreous by atrophy of vasa hyaloidea propria. A line of condensation appears, separating the central vascular remains of the early vitreous, which ceases to grow after the 40 mm. stage, from the peripheral avascular secondary vitreous. Stage of formation of Cloquet's canal and the capsula perilenticularis or anterior portion of the hyaloid membrane. This stage ends with the appearance of the ciliary region roughly between 50 and 60 mm.

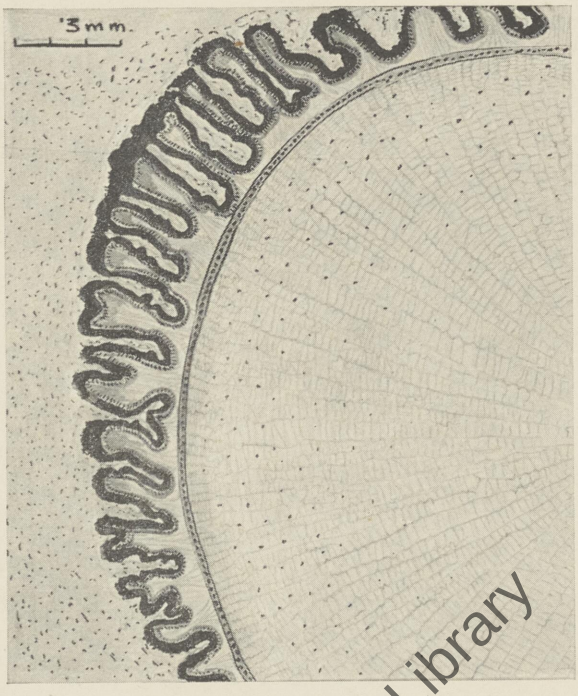


Fig. 156. Equatorial section through a foetal lens (110 mm.). The ciliary processes and the bundles of fibres of the suspensory ligament are also seen.

3. **Third period**, from 65 mm. onwards (3rd to 6th month). Formation of *tertiary vitreous* from neural ectoderm of ciliary region, and differentiation of this to form zonule fibres. Atrophy of the "faisceau isthmique" of Druault and formation of the lateral condensation between secondary and zonule fibres, namely the "lateral part of the anterior hyaloid membrane." This stage ends when the secondary vitreous is completely marked off from the tertiary.

Thus we see that the adult vitreous is practically entirely derived from the neural ectoderm of the inner layer of the optic cup, only that portion lying immediately behind the lens and in the neigh-

Digitized by Illinois College of Optometry Library

bourhood of the canal of Cloquet having in it any element derived from surface ectoderm (lens) or mesoderm.

Fig. 157 represents these three stages diagrammatically. A fourth stage may be added (post-natal).

4. **Post-natal development of the vitreous.** To these three embryonic periods of vitreous development may be added a fourth which covers the first three or four years after birth. The changes

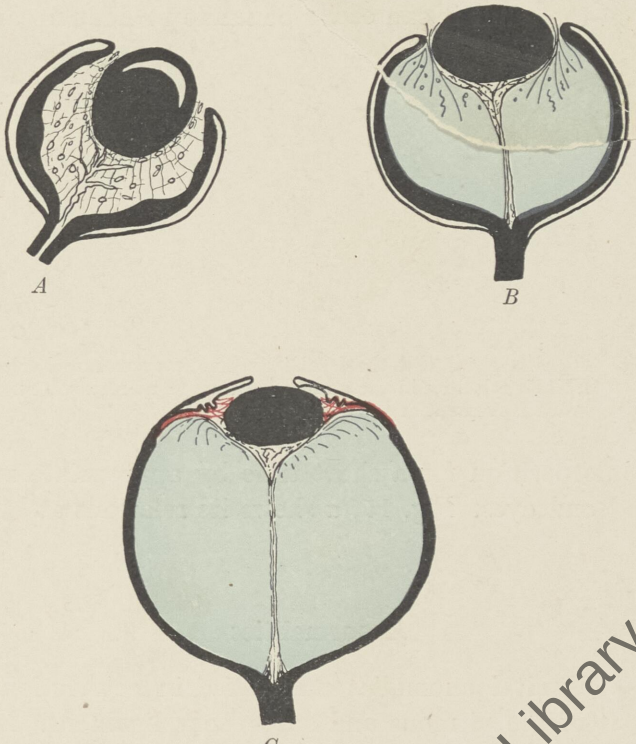


Fig. 157. Diagram of the three stages of vitreous development. *A*, 1st stage. The vasa hyaloidea propria are filling the vitreous. *B*, 2nd stage. The vasa hyaloidea propria are atrophying and the secondary vitreous (blue) is forming. *C*, 3rd stage. The "tertiary vitreous" (red) is apparent.

which occur during this period are concerned solely with the relationships of Cloquet's canal and the anterior end of the hyaloid artery. At birth Cloquet's canal extends horizontally backwards from a point a little below and to the nasal side of the posterior pole of the lens to the optic disc. The extreme anterior end of the main trunk of the hyaloid artery extends horizontally backwards from the lens capsule along the first part of the canal. After birth further atrophy involves this vascular remnant and it gradually drops until it comes to hang down perpendicularly from the lens. It also becomes curled into a

Digitized by Illinois College of Optometry Library

spiral form. At the same time the walls of Cloquet's canal become very lax and the whole structure tends to sag down so that its anterior open mouth, instead of pointing straight backwards, comes to lie well below the posterior pole of the lens and finally on a level with the lower border of the dilated pupil. It is thus not obvious in the living eye in the upright position, though the backward slope of the vitreous face seen with the slit-lamp is an indication of its continued presence in the lower part of the eye. Its walls remain extremely slack and in the adult it can easily be made to float up and assume

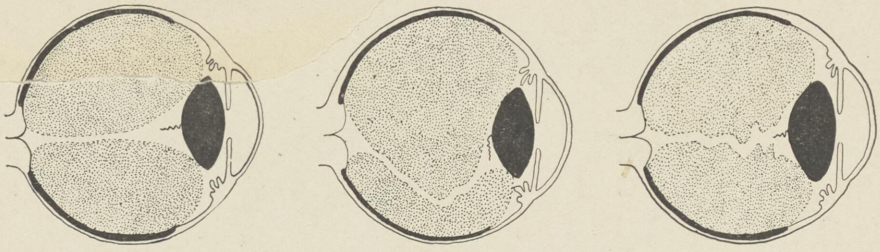


Fig. 157 *a*. *A*, Cloquet's canal and the hyaloid remnant extending horizontally backwards at birth. *B*, Their relations in the adult with the eye at rest. *C*, Their relations in the adult after upward movement of the eye.

its embryonic position for a short time by appropriate movements of the head and eyes. Fig. 157 *a* shews its relations at birth and in the adult.

Abnormalities

Certain congenital anomalies may arise in connection with the development of the vitreous and suspensory ligament. In the first place, in malformed eyes, and especially in those in which the anomaly seems to point to abnormality of closure of the foetal fissure, the vitreous may be cellular. It may contain fibrous tissue, sometimes very dense, and occasionally fatty tissue and even bone. These three tissues are obviously due to atypical differentiation of the mesoderm around the hyaloid artery. No abnormality of the ectodermal portion is known. It may, of course, be absent altogether in extremely microphthalmic eyes filled with mesoderm.

Anomalies of differentiation of the zonule may lead to abnormalities of the lens. The equal pull of the zonule fibres would appear to modify the shape of the growing lens, since, if the zonule fails to develop over any region, the corresponding segment of the lens will be shorter and thicker than normal and give rise to the appearance

Digitized by Illinois College of Optometry Library

of a notch (coloboma lentis). In cases where the zonule is absent over a large area the lens may be pulled towards the opposite side and a congenital dislocation result. The same thing will result if the fibres are tougher and shorter on one side than the other, even if they are nowhere absent.

The amount of condensation of the so-called hyaloid membrane and the fibrils in the vitreous would appear to vary extremely in perfectly normal eyes, as also do the shape, size and number of the vascular remnants which can be traced on the back of the lens. At present the limits of the normal in this respect have not been fully worked out.

Digitized by Illinois College of Optometry Library

VI

THE ASSOCIATED MESODERM

A. The Foetal Blood System and the Mesodermal Portion of the Iris

Under the heading of "the foetal blood system" must be described:

1. The development and arrangement of the larger blood vessels in the orbit, supplying or draining the optic cup.
2. The development of the choroid.
3. The development and retrogression of the foetal intra-ocular blood system (i.e. the hyaloid artery, the tunica vasculosa lentis and their connections) and the differentiation of the vessels of the iris and ciliary body.
4. The development of the definitive retinal arteries and veins.

1. The Development and Arrangement of the Larger Blood Vessels in the Orbit, supplying or draining the Optic Cup

Vessels containing nucleated red blood cells can be recognised easily in the mesoderm surrounding the optic vesicles of the youngest embryos examined. At the 5 mm. stage the arrangement of the spaces is that shewn in Fig. 158. It will be seen that a carotid artery is present, lying beside the brain and curving over the short optic stalk, and that a branch from this comes into relation with the lower aspect of the optic vesicle. This branch is also connected with vessels on the surface of the visceral mesoderm of the maxillary process.

It must not be supposed from the foregoing description and figure that there is at this early stage a differentiation of blood vessels into arteries and veins. The nature of the respective channels can only be inferred from their position, no mesodermal wall other than a single layer of flattened cells being present in any of them.

Fig. 159 shews the appearance of a typical blood channel of a 4·5 mm. embryo.

The optic vesicle at the 4·5 mm. stage is just beginning to invaginate from the lower and outer side to form the optic cup, and the branch from the carotid runs along the under side of the optic stalk in relation to the depression in this which will become the foetal fissure. The blood channels form a sort of plexus rather than a single vessel, and one branch of this is becoming included within the lips of the deepening foetal fissure and so finding its way inside

Digitized by Illinois College of Optometry Library

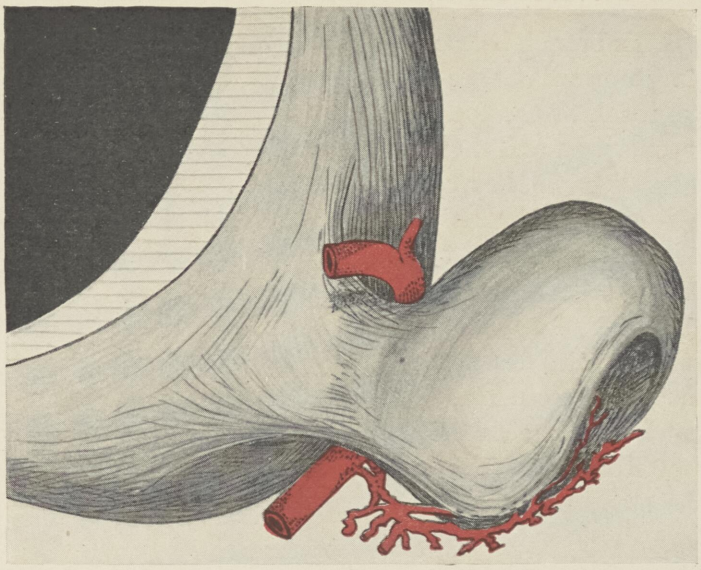


Fig. 158. Reconstruction of the optic cup of a 5 mm. human embryo seen from the front. The large vessel passing up behind the optic stalk and curving forwards above this is the internal carotid. Two main vessels can be seen below the cup; one, the future hyaloid artery, is already penetrating into the interior of the cup, the other is vascularising its margin.

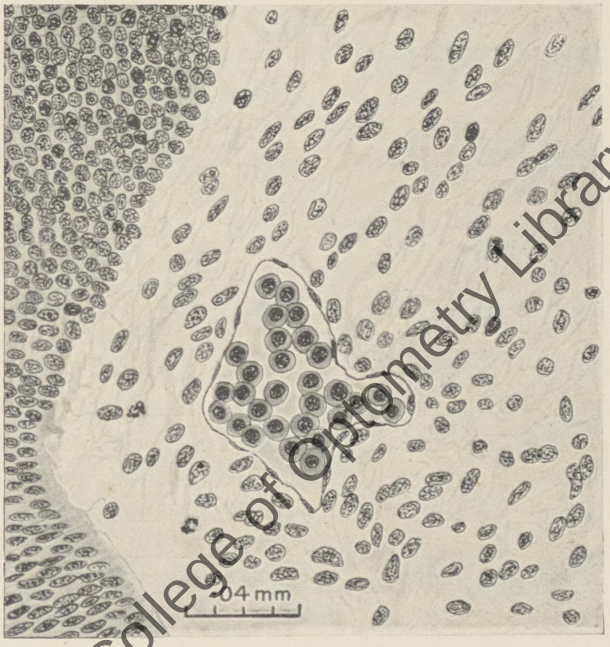


Fig. 159. Transverse section across the internal carotid artery of a 4·5 mm. human embryo. The vessel wall is a single layer of endothelium and the erythrocytes are nucleated.

Digitized by Illinois College of Optometry Library

the cup. This branch is known as the *hyaloid artery*. Other branches are passing upwards along the margins of the cup. They do not at this stage reach to the top of the cup, so that the upper part of this is not vascularised and there is no choroidal network over the outside (though small capillaries can be found in contact with it here and there). Neither is there at this stage any pigment in the outer layer of the cup. The vessels of the chorio-capillaris and the pigment in the neural ectoderm appear to develop *pari passû*, and there is a certain amount of evidence that there is some interaction between them. It is certain, at any rate, that no chorio-capillaris develops in situations where mesoderm is in contact with neural ectoderm which is unpigmented. The slightly older embryo seen in Fig. 158 exhibits these same features.

At this stage the only blood vessels in contact with the optic vesicle are derived from the carotid artery and can therefore be looked on as the earliest representatives of the ophthalmic artery and its branches. The venous side of the ocular circulation begins almost immediately after this, when small blood spaces can be recognised in the orbital mesoderm. These coalesce to form venous channels draining ultimately into the *cavernous sinus*.

Pigment begins to appear in the outer layer of the optic cup at 5–6 mm. and at this time minute blood spaces containing a few nucleated cells can be found more or less all over the outside of the eye. The larger "arterial" vessels below the stalk extend further upwards along the margin of the cup. At this stage the presence of an *anterior cerebral plexus* of blood spaces can be made out, lying along the outer part of the anterior cerebral vesicle and communicating with a larger space lying on the inner side of the Gasserian ganglion, i.e. the future cavernous sinus. The small vessels which ramify in the orbital mesoderm and help to form the vascular network in contact with the optic cup communicate with this plexus.

The upward growing vessels on the margin of the optic cup finally meet and join at the top so that a complete vascular circle is formed by the 13 mm. stage or earlier. Fig. 160 shews the front view of a model of the eye of a 10 mm. embryo in which the branches have not quite met. The vascular circle is complete except at *a* where there is a small gap. The chorio-capillaris now forms a complete network over the outside of the eye and this net communicates anteriorly with the vascular circle, now called the *annular vessel*, which is supplied with blood from the hyaloid artery (now included within the optic cup by closure of the foetal fissure). The branches of the hyaloid which communicate with the annular vessel can be

Digitized by Illinois College of Optometry Library

seen appearing round the margin of the optic cup in Fig. 160 and also passing out through the, as yet, open anterior end of the foetal fissure. As the annular vessel also communicates by several branches with the developing choroidal net on the outside of the eye, it is a moot point whether it should be considered as arterial (formed by the anastomosis round the margin of the cup of the distal branches of the arteria hyaloidea) or as venous and representing merely the enlarged loops of the general choroidal net. It was described by Fuchs originally as an artery and subsequently by Versari as a vein, but it is perhaps better, in view of the peculiarities of the ocular circulation[1], to call it merely the *annular vessel*.

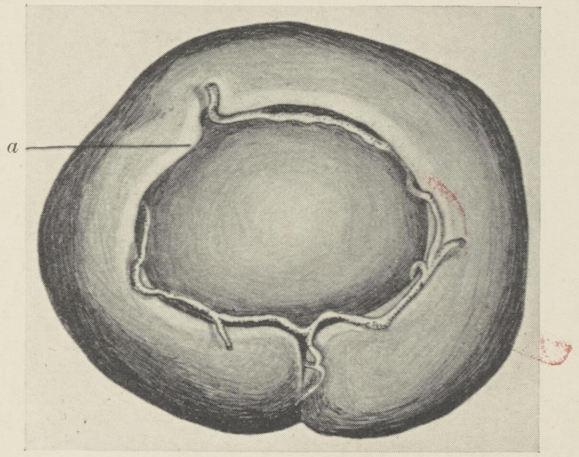


Fig. 160. Model of the eye of a 10 mm. human embryo seen from the front. The annular vessel is seen around the margin of the cup, and vessels are seen passing from this between the margins of the cup and the lens to join the hyaloid artery behind the lens. The foetal fissure is seen below. *a*, gap in annular vessel.

The chorio-capillary net communicates proximally by several scattered channels with two main blood spaces, the *supra-orbital* and the *infra-orbital plexus*, which lie respectively above and below the optic vesicle and which both eventually drain into the cavernous sinus. Fig. 161 shews in a diagrammatic way the state of affairs in a 13 mm. embryo. The outside of the cup is covered by a capillary net which communicates by two main (and possibly other) branches, below with the infra-orbital plexus and above, by two branches, with the supra-orbital plexus. The internal carotid artery is seen passing upwards behind the optic stalk. It gives a branch (the

[1] Even in the adult eye arteries pass in many places directly into veins and no division can be made.

Digitized by Illinois College of Optometry Library

arteria ophthalmica interna) which runs along the lower part of the stalk and enters the eye through the foetal fissure. The intra-ocular portion is the *hyaloid artery*, and this anastomoses by branches round the margin of the cup with the annular vessel as before. No other vessels definitely arterial in nature can be seen in the orbit at this stage, and the direction of the blood flow in the chorio-capillaris and the four vessels communicating with it is problematical (see p. 36).

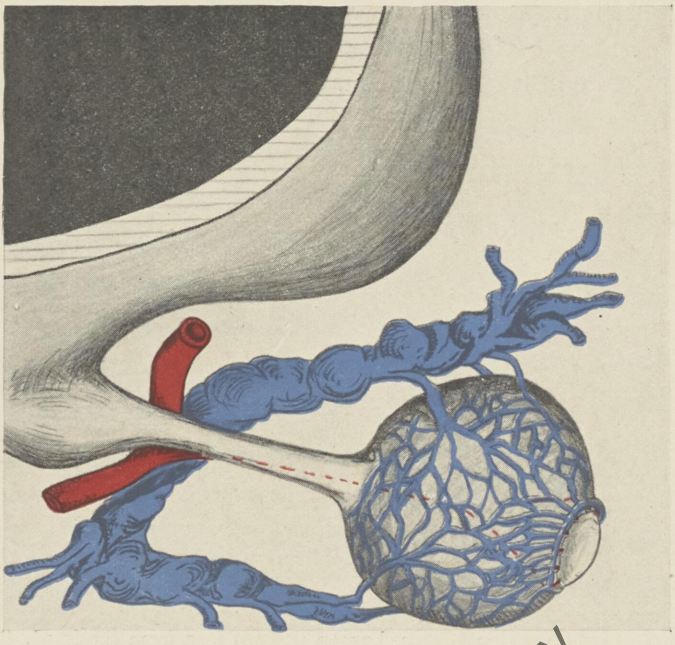


Fig. 161. Reconstruction of the eye and part of the fore-brain of a 13 mm. human embryo, seen from the front. The internal carotid artery is seen passing up behind the optic stalk and giving a branch, the hyaloid artery, along the under surface of this to enter the eye. The venous plexuses above and below the eye drain the choroidal net which is connected anteriorly with the annular vessel and so with the terminal branches of the hyaloid artery passing round the margin of the cup.

The vessels corresponding to the arterial side of the definitive choroidal circulation are not recognisable until the 18 mm. stage, at which time the original channels of communication with the large plexuses can be seen to represent the *venae vorticosae* draining respectively into the superior and inferior ophthalmic veins, and so ultimately into the cavernous sinus.

Fig. 162 shews the condition at 16 mm. It is similar to the 13 mm. stage but the large sinuses are more definite in outline and their tributaries form two main trunks, each of which divides on nearing the globe. The *arteria ophthalmica interna* can now be seen to have

Digitized by Illinois College of Optometry Library

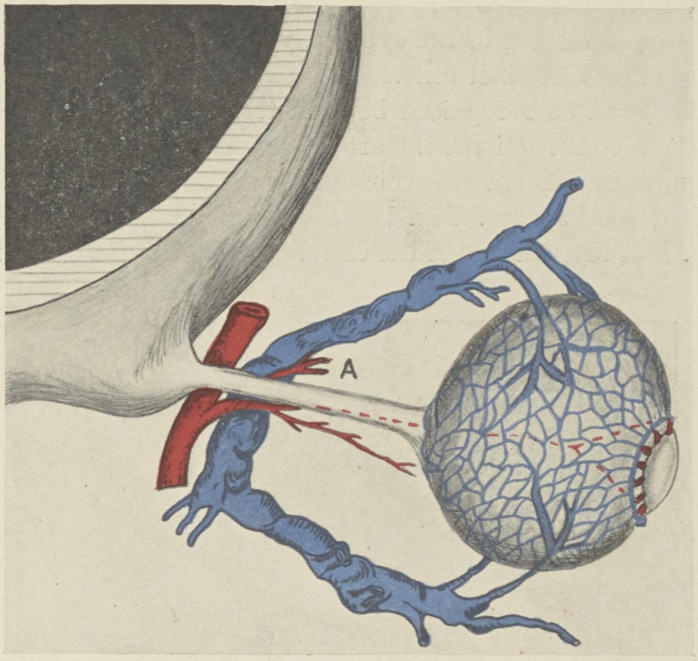


Fig. 162. Reconstruction of the eye of a 16 mm. human embryo seen from in front. The internal carotid gives off the arteria ophthalmica interna, which now gives off a branch passing up behind the optic stalk and another smaller one running towards the nasal side of the cup, as well as the hyaloid artery. The veins are much as before. *A*, common ciliary artery.

three branches, one, the original hyaloid, still enters the eye through the foetal fissure. Another, the beginning of the common ciliary artery, passes upwards on the temporal side of the optic stalk, while

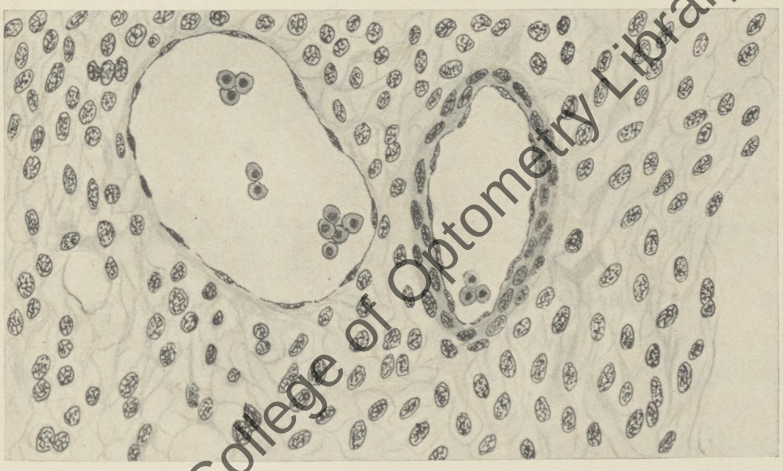


Fig. 163. Transverse section through an artery (right) and a vein (left) in a 16 mm. human embryo.

Digitized by Illinois College of Optometry Library

a third, formed of rather indefinite anastomosing channels, passes towards the nasal side of the eye (early nasal ciliary).

There is now a distinct difference between the walls of arteries and veins. This can be recognised both in transverse section (Fig. 163) and in the reconstructions, the arteries appearing small and discrete, with a uniform lumen, the veins still being composed of irregular coalescing blood spaces. Fig. 164 shews the condition in an 18 mm. embryo. The arterial side of the circulation is now quite well marked.

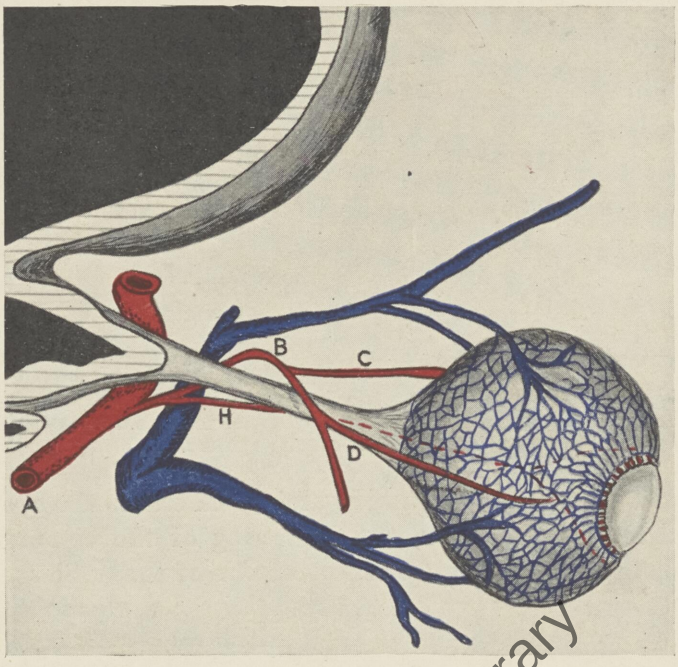


Fig. 164. Reconstruction of the eye of an 18 mm. human embryo. *A*, internal carotid *B*, common ciliary artery; *C*, temporal long ciliary artery; *D*, nasal long ciliary artery; *H*, hyaloid artery.

The arteria ophthalmica interna appears to divide into two branches. One of them is the *hyaloid* and enters the stalk as before, the other can now be called the *common ciliary*. It is a continuation of the upper branch seen in Fig. 162 and now gives off the *temporal ciliary* artery, which passes to the temporal side of the cup and finally becomes the *temporal long ciliary artery* of the adult. The main trunk of the common ciliary crosses above the nerve from the temporal to the nasal side and anastomoses with the small branch (*early nasal ciliary*) seen on the nasal side in the previous stage. The original connection of this with the arteria ophthalmica interna disappears

Digitized by Illinois College of Optometry Library

and the vessel becomes the *nasal* of the two *long ciliary arteries*. The main trunk of what was the common ciliary goes on towards the ethmoidal region.

The annular vessel by this time has decreased in relative size and become merged into the choroidal net. Its place finally becomes taken by the secondary anastomosis between the terminal branches of the nasal and temporal long ciliary arteries (Versari). A second vascular circle is thus formed at the margin of the cup, and this, both from its mode of development and from its structure, can be labelled definitely as arterial.

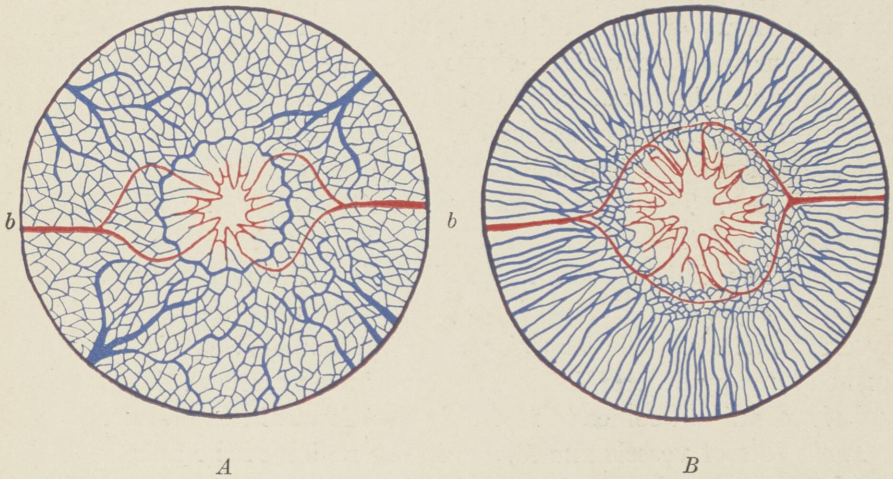


Fig. 165. *A*, the anterior portion of the choroid and pupillary membrane at the 25 mm. stage, after the appearance of the long ciliary arteries but before their anastomosis. The annular vessel is seen in blue in the centre and the long ciliary arteries at *b*, *b*. The large radial veins are tributaries of the venae vorticosae. *B*, the same region after formation of the anastomosis between the long ciliary arteries. The annular vessel is no longer distinct.

Fig. 165 shews the vessels of the region of the margin of the cup just before and just after the formation of the anastomosis between the nasal and temporal long ciliary arteries. Branches of these join the capillary net-work at the posterior part of the globe and form the *posterior ciliary arteries*. The original channels of drainage into the supra-orbital and infra-orbital plexuses are now the *venae vorticosae*, draining into the *superior* and *inferior ophthalmic veins*. Of the arteries, the adult condition is reached as follows:

The main trunks of the nasal and temporal ciliaries form the *long ciliary arteries*, anastomosing as the *circulus arteriosus iridis major* in the *base* of the iris, while their branches form the *posterior* ciliaries. The proximal part of the arteria hyaloidea forms the *intra-neural* portion of the *arteria centralis retinae*, its distal portion atrophies.

Digitized by Illinois College of Optometry Library

The branches of the arteria centralis retinae develop as off-shoots from the main trunk of the hyaloid artery as it passes through the nerve head, and will be described in detail later.

Thus the main vessels supplying or draining the optic cup may be divided developmentally as well as anatomically into two sets:

(*a*) *Arterial.* These appear first. They are derived from the *internal carotid* artery. This gives a branch, the *arteria ophthalmica interna,* which enters the optic cup and vascularises its margins and its interior (hyaloid artery and, later, arteria centralis retinae). Later, external branches (the nasal and temporal branches of the common ciliary artery) arise and these in turn break up to form the posterior and long ciliary arteries and the circulus arteriosus iridis major. The description and figures given above of the process must not be taken as absolute. The exact points of division and the arrangement of the arteries in the early stages are subject to individual variations, but the general plan is usually that given above.

(*b*) *Venous.* These vessels appear a little after the inception of the arteria ophthalmica interna, and form a net on the outside of the cup (the primitive choroid). This drains via the venae vorticosae into the *supra-orbital* and *infra-orbital* plexuses and so into the cavernous sinus. The *superior* and *inferior ophthalmic veins* are formed later by differentiation of some of the vessels of the plexuses, and the condition comes to resemble that found in the adult.

These sets of vessels *anastomose* in the region of the margin of the cup by channels (larger than capillaries) which cannot be classified as either arteries or veins. The earliest of these is the *annular vessel.* Others appear subsequently and will be described in dealing with the circulation in the iris.

2. The Development of the Choroid.

The network of capillaries described above as encircling the optic cup at an early age (6 mm.) can be looked upon as part of the general surface-vascularisation of the central nervous system. We have seen that very early indeed, before the invagination of the optic vesicle, minute capillaries can be found in contact with the walls of the nerve tube everywhere. Some of these penetrate into the neural ectoderm and form the earliest blood supply of the brain. Others merely ramify on the surface. We have noted, in considering the early stages of retinal development, that the wall of the optic vesicle shares for a time in this capillary blood supply. It is most marked on the thickened lower and outer part of the vesicle, where invagination is

Digitized by Illinois College of Optometry Library

just commencing, and is absent over the upper part of the vesicle, where the wall is thin and destined to form the outer layer of the optic cup. It is not until the appearance of pigment here, at 8–10 mm., that anything approaching a continuous vascular network is found in contact with the outer surface of the optic cup, and even then the vessels do not appear ever to penetrate the ectodermal wall in the way that they do in the invaginating region. This appears to be correlated with their different origin in the two situations. In the region of the future foetal fissure the penetrating capillaries are derived from vessels belonging to the internal carotid system (hence potentially arterial), while in the upper part of the cup the capillaries are associated from the first with venous plexuses connected with the cavernous sinus.

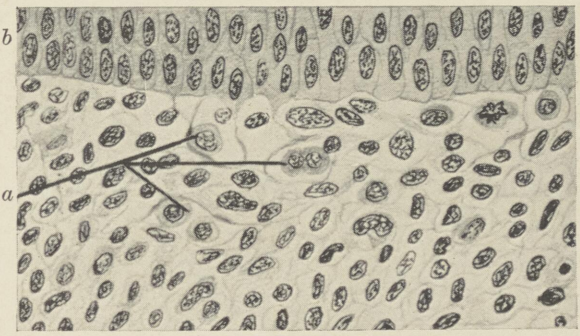


Fig. 166. Section shewing the edge (*b*) of the outer layer of the optic cup at 5 mm. Processes from its cells join up with processes from mesoderm cells. Among these latter are indefinite spaces containing foetal erythrocytes (seen at *a*).

The commencing choroidal net at 5 mm. has the appearance seen in Fig. 166. It will be noted that the vessels are mere endothelial tubes. They have no adventitia and the mesoderm of their walls is continuous by means of fine fibrils with the cells of the surrounding mesodermal stroma and also with the ectodermal cells of the wall of the optic vesicle. This is merely an expression of the marked continuity of protoplasm which is general throughout the embryo at this stage.

After the appearance of the ectodermal pigment the choroidal net increases rapidly; it becomes richer and the component vessels more conspicuous. At the same time the continuity between the ectoderm of the pigmented wall of the optic cup and the surrounding mesoderm is lost and a distinct basement membrane can be found separating the two. This by the 14 mm. stage is recognisable as a definite glass membrane, the *membrane of Bruch*.

Digitized by Illinois College of Optometry Library

Fig. 167 shews the pigment epithelium and adjacent choroid in a 10 mm. embryo. It will be seen that there is no sign of continuity between them. At this stage the choroid presents the rudiment of the *chorio-capillaris* and the membrane of Bruch. There is as yet no sign of the outer layers of larger vessels or of the lamina supra-choroidea. The connections of the net of capillaries at this stage are two, namely:

1. Directly with larger vessels forming part of the supra-orbital and infra-orbital plexuses, and

2. Via the annular vessel with branches of the arteria hyaloidea within the cup. A few small direct anastomoses between choroid and hyaloid artery can be found along the foetal fissure until this closes completely at 12 mm. when they are naturally cut off.

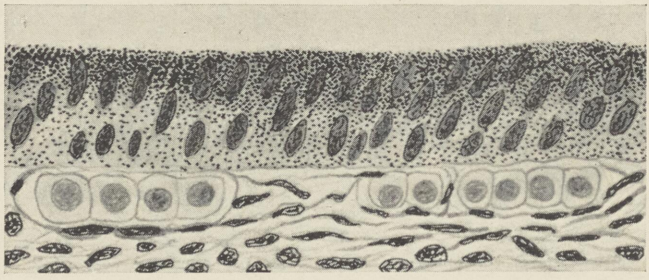
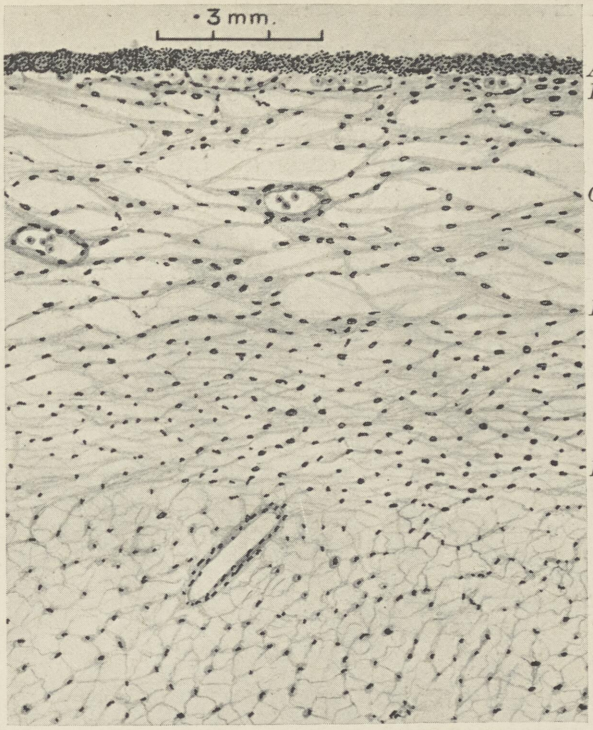


Fig. 167. Section through the pigment epithelium and the adjacent capillaries of the choroid of a 10 mm. human embryo. Pigment is present and the capillaries are much more numerous, more regular and better defined than they were at 5 mm.

At this stage, although the choroid definitely drains into the large venous plexuses above and below the eye, there is not visible any definite layer of larger vessels formed by tributaries of the venae vorticosae, such as occurs in the adult. This layer can be recognised with certainty at the *3rd month*, at which time the scleral condensation is so far advanced that a definite separation (in the line of the future *lamina supra-choroidea*) between it and the choroid can be seen. This second layer of choroidal vessels is venous in nature, composed of relatively large vessels, and represents the outermost layer of the three usually described in the adult. Just before it appears (i.e. during the 2nd month) the capillaries towards the anterior portion of the cup become arranged in parallel lines, passing from behind forwards towards the margin, in the region of which they tend to break up into a network again. (This is seen in Fig. 165 *B*.)

Fig. 168 shews a section through the choroid of a 65 mm. embryo

Digitized by Illinois College of Optometry Library



about 12 wks
3 months

Fig. 168. Section through the choroid and sclerotic of a 65 mm. human embryo. *A*, pigment epithelium of retina; *B*, chorio-capillaris; *C*, layer of larger vessels (venous); *D*, inner surface of sclerotic condensation; *E*, outer surface of sclerotic condensation.

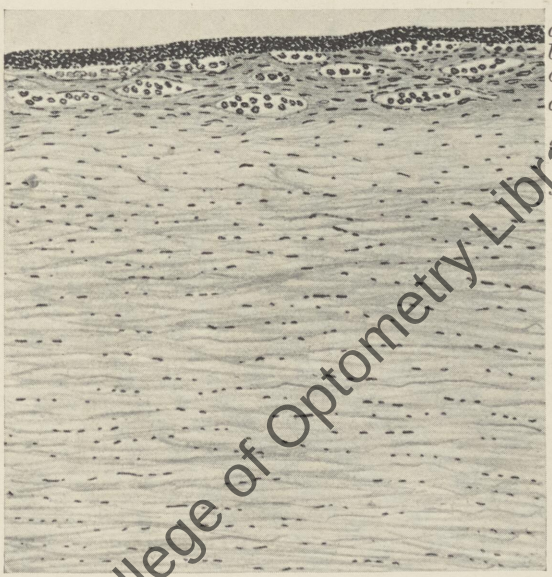


Fig. 169. Section through the choroid and sclerotic at 5 months. *a*, pigment epithelium of retina; *b*, chorio-capillaris; *c*, intermediate layer of vessels (arterial); *d*, outer layer of vessels (venous); *e*, lamina supra-choroidea; *f*, inner surface of sclerotic.

Digitized by Illinois College of Optometry Library

(3 months). It will be seen that the chorio-capillaris can be clearly recognised, that outside this is a tissue of looser mesh in which are appearing some larger venous channels, tributaries of the venae vorticosae. This loose tissue ends at the inner surface of the sclerotic condensation in the line of the future lamina supra-choroidea.

The middle layer of vessels recognisable in the adult choroid spreads from the region of supply of the short ciliary arteries. It is arterial in nature. The vessels are branches of ciliary arteries breaking up to supply the chorio-capillaris. They are first recognisable at about 4 months and the layer spreads rapidly from behind forwards.

By 5 months the choroid presents the appearance seen in Fig. 169. All the layers present in the adult are distinguishable; the choroid is well separated off from the sclerotic and at this stage, for the first time, chromatophores (pigment-bearing cells) can be recognised in it. It differs from the adult choroid, however, in having a much more richly nucleated stroma. The first chromatophores appear in the outermost layer and pigmentation gradually spreads inwards. It will be remembered that, even in the adult, pigment cells are more numerous next the sclera than in the inner layers. At birth the choroid resembles that of the adult save that it is rather more cellular.

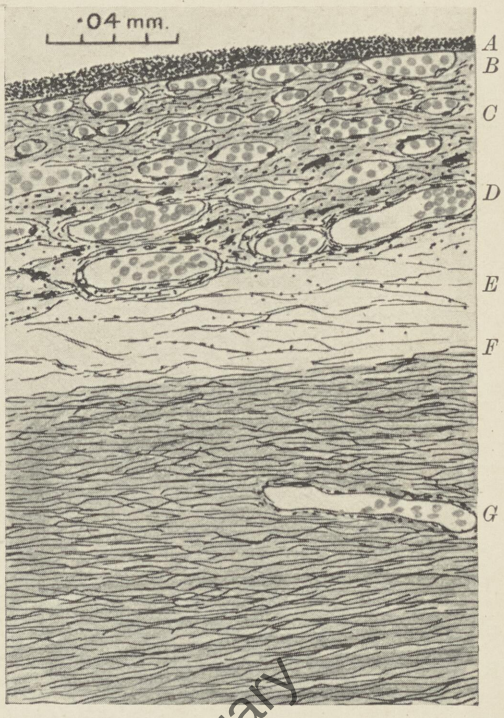


Fig. 170. Section through the choroid at 7 months. *A*, pigment epithelium of retina; *B*, chorio-capillaris; *C*, intermediate layer of vessels; *D*, large veins; *E*, lamina supra-choroidea; *F*, inner surface of sclera; *G*, perforating vessel in sclera.

Fig. 170 represents the choroid at 7 months, and Fig. 171 the choroid at birth in a foetus in which all the vessels were abnormally dilated.

Digitized by Illinois College of Optometry Library

3. **The Development and Retrogression of the Foetal Intra-ocular Blood System** (i.e. the hyaloid artery, the tunica vasculosa lentis and their connections) and the differentiation of the vessels of the iris and ciliary body.

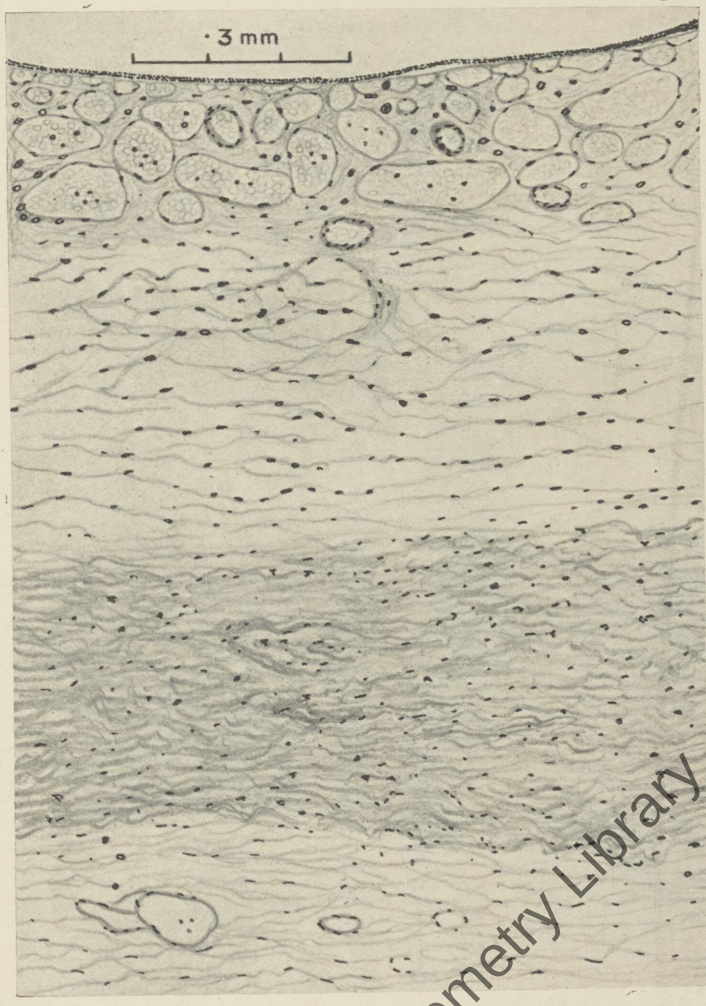


Fig. 171. Section through choroid (term) in which the vessels are abnormally dilated. Arteries can be distinguished from veins by their thicker walls. The lamina suprachoroidea (*l*) is wide. The sclera (*s*) is more cellular than and not so thick as it is in the adult.

The hyaloid artery, as we have seen, is at first the distal portion of the main trunk of the ophthalmica interna branch of the internal carotid. Later, when (10 mm.) a continuation of the artery outside the optic cup can be recognised, the hyaloid comes to be described as a branch of the ophthalmic, and not the terminal portion of its main trunk. It enters the optic cup by running along the groove

Digitized by Illinois College of Optometry Library

which marks the beginning of the foetal fissure at 5 mm. At first, while the fissure is completely open, it communicates along the whole length of this with small capillary vessels lying in the mesoderm below the eye and continuous with the capillary net forming the primitive choroid. The connections with the extra-ocular blood system become cut off one by one as the fissure closes, those at the distal end remaining longest since this is the last portion of the fissure to close. The terminal part of the main hyaloid appears in early specimens (6–7 mm.) to end in the neighbourhood of the posterior part of the lens thickening in a fine fibrillated tissue containing a few stellate vasoformative mesoderm cells. This tissue, part mesoderm, part

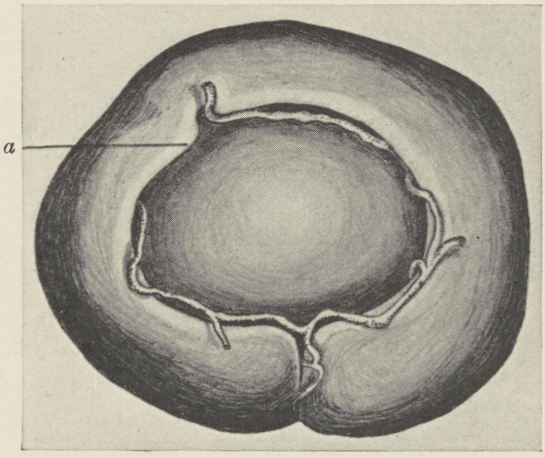


Fig. 172. Model of the eye of a 10 mm. human embryo seen from the front. The annular vessel is seen around the margin of the cup, and vessels are seen passing from this between the margin of the cup and the lens, to join the hyaloid artery behind the lens. The foetal fissure is seen below. *a*, gap in annular vessel.

ectoderm of the primitive vitreous, comes to form, when the lens vesicle separates, the *capsula perilenticularis fibrosa*. In the meshes of this the hyaloid artery extends by throwing out small buds which, becoming capillaries in their turn, form a vascular net over the posterior surface of the lens, at first inside and later practically replacing the capsula perilenticularis. This is the beginning of the *tunica vasculosa lentis*. Its posterior part can be recognised at 8–9 mm. At first the vessels composing it (branches of the hyaloid artery) only communicate with extra-ocular vessels in the line of the cleft, namely below the lens vesicle, but at 10 mm. or earlier two other channels can be recognised on either side of the lens vesicle. These are seen in Fig. 172, which shews the annular vessel into which they run. At this stage, therefore, the intra-ocular blood system con-

Digitized by Illinois College of Optometry Library

sists of a hyaloid artery, thin-walled and with a somewhat irregular lumen, which enters the eye at the upper part of the fissure and runs towards the posterior pole of the lens vesicle. Here it breaks up into three main sets of capillaries, an inferior, a nasal and a temporal set. The inferior set is at first the largest, running downwards below the lens vesicle and passing out of the eye at the still open anterior end of the foetal fissure to anastomose with choroid vessels. They pass between the margin of the optic cup and the equator of the lens vesicle and run into the annular vessel, which at this stage is forming

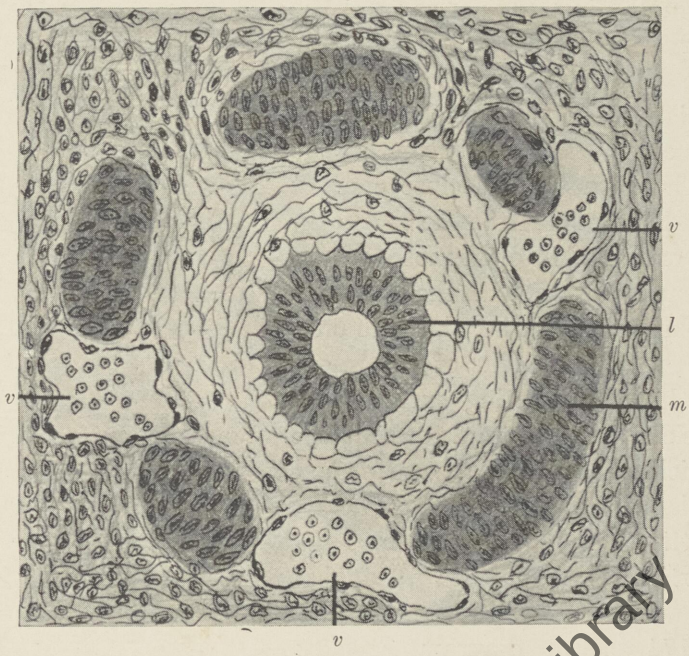


Fig. 173. Equatorial section (after Bach and Seefelder) of the margin of the optic cup of an 8·3 mm. human embryo. *v*, vessel indenting margin of cup *m*; *l*, lens vesicle; *m*, margin of optic cup.

around the edge of the cup. As they pass over the edge of the cup they indent it very slightly. This is seen in Fig. 173, which shews an equatorial section of the rim of the optic cup in an 8·3 mm. human embryo. The three vessels passing out of the cup are seen indenting the edge respectively below and on either side. Mesoderm (where later other capillaries will appear) is seen indenting the margin in two other situations as well. These three anastomoses between the intra-ocular and extra-ocular blood systems can be looked upon as the earliest formed parts of the *lateral* or *capsulo-pupillary* portion of the tunica vasculosa lentis. Between the three vessels the space

Digitized by Illinois College of Optometry Library

between the equator of the lens vesicle and the edge of the optic cup is occupied by fine strands of mesoderm which connect the mesoderm outside the eye with that forming the walls of the hyaloid artery. These strands are in intimate protoplasmic continuity with the ectodermal fibrils of the primitive vitreous, and together they form the condensation known as the *capsula perilenticularis fibrosa*. Very soon after the 10 mm. stage this tissue surrounding the lens becomes vascularised by further branches from the hyaloid artery, and a series of straight channels is formed, connecting the hyaloid with the annular vessel and so with the choroid. A little later (17 mm.) a few small blind buds arise from the annular vessel itself and begin to vascularise the mesoderm, which (after separation of the lens vesicle from the surface ectoderm) lies in front of the lens. These buds lie in close contact with the lens vesicle from the beginning and never extend into the mesoderm so as to come in contact with the ectoderm of the surface itself, i.e. they are only among the deepest cells of the mesodermal layer separating surface and lens vesicle. They extend towards the lens vesicle and by 25 mm. have formed a vascular covering for this, and constitute therefore the *anterior* or *pupillary portion* of the tunica vasculosa lentis.

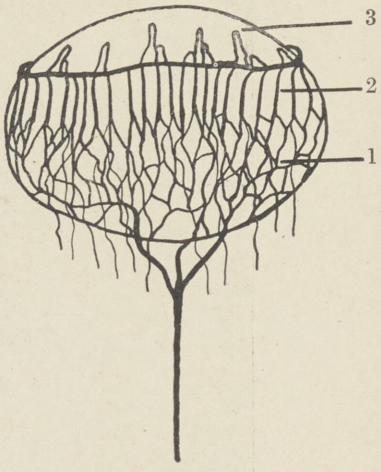


Fig. 174. Diagram shewing the relation of the three parts of the tunica vasculosa lentis to the lens vesicle. 1, posterior portion of the vascular capsule of lens; 2, lateral or capsulo-pupillary portion; 3, anterior portion or pupillary membrane.

Fig. 174 shews diagrammatically these three parts of the tunica vasculosa lentis and their connections. The direction of the blood in the anterior capillary loops is problematical. That in the posterior portions of the tunica is from behind forwards. Few, if any, of the anterior loops run across the front of the lens: most of them approach the anterior pole and then, forming an acute bend, turn back upon themselves and rejoin the annular vessel within the same quadrant in which they arose.

Whether or not this arrangement is primarily due to their beginning to arise at a time when the presence of the lens stalk would hinder their passage from side to side is doubtful, since they can only be recognised with certainty *after* separation of the lens vesicle.

By 13 mm. the posterior and lateral parts of the tunica vasculosa lentis are well established. Fig. 175 shews a reconstruction of the

Digitized by Illinois College of Optometry Library

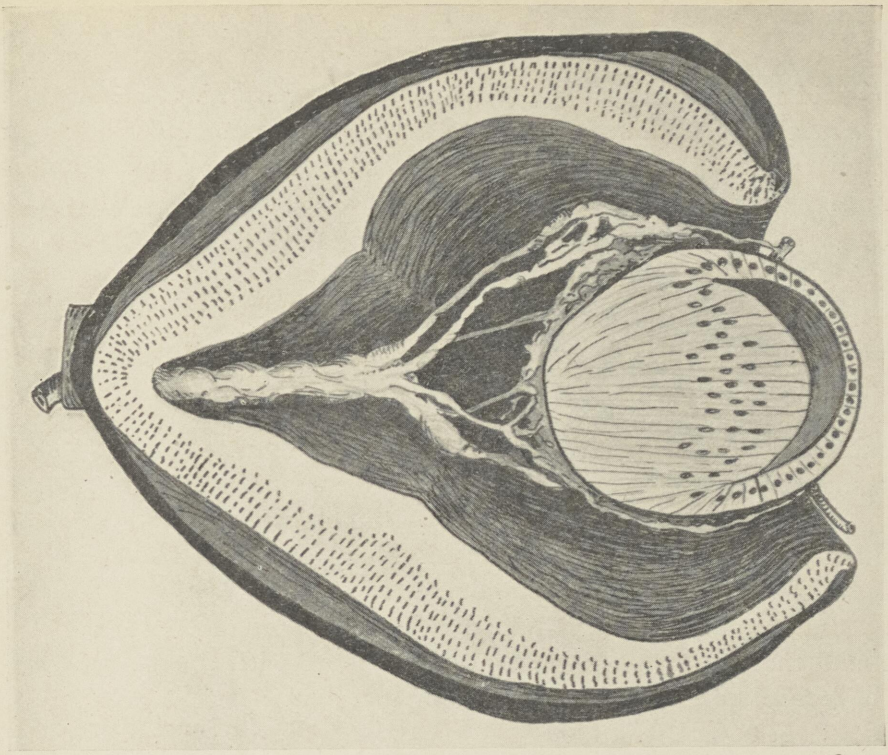


Fig. 175. Reconstruction of half the optic cup and contents in a 13 mm. human embryo. The hyaloid artery is seen breaking up into branches which pass to the back of the lens. Small channels (capsulo-pupillary) unite these with the annular vessel which can be seen cut at the margin of the cup on either side of the lens vesicle.

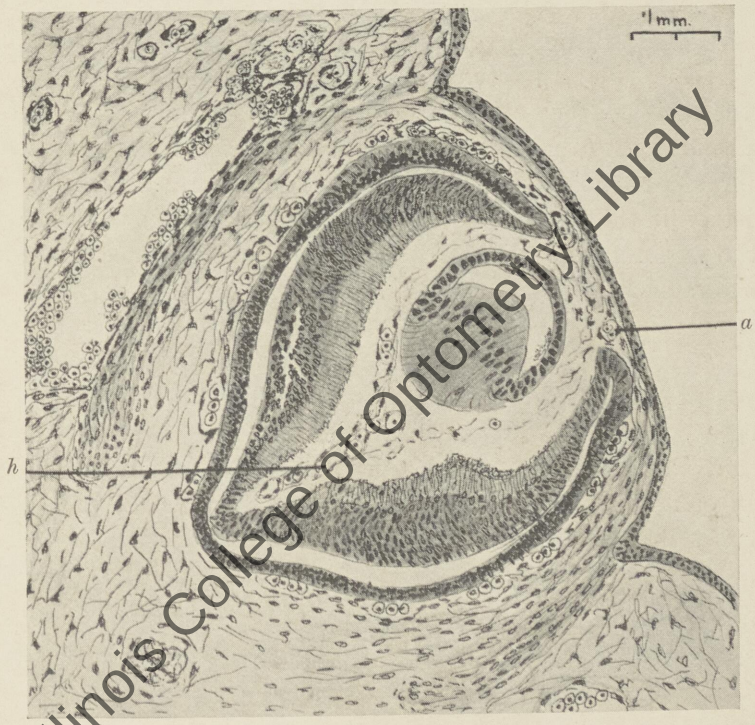


Fig. 176. Section through the eye of a 13 mm. human embryo. *a*, annular vessel; *h*, main trunk of hyaloid.

Digitized by Illinois College of Optometry Library

hyaloid system and its connections at this stage. Fig. 176 shews one of the sections from which the reconstruction was made. It will be seen that the main hyaloid vessel now breaks up into branches before it reaches the back of the lens. The number in this embryo was five, but this is probably variable.

Fig. 177 shews them as they appear in the reconstruction of an equatorial section 0·018 mm. in front of the point of entry of the hyaloid. At this stage the hyaloid artery gives no other branches than these which pass directly to the back of the lens and take part in the formation of its vascular capsule. Two parts of this can now be recognised, namely:

1. The posterior portion formed by the breaking up of the main trunk of the hyaloid.

2. The lateral or capsulo-pupillary portion formed by straight unbranched palisade-like vessels passing round the equator of the lens to anastomose with the annular vessel. The anterior or pupillary portion is not yet apparent.

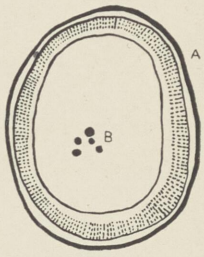


Fig. 177. Reconstruction of an equatorial section through the eye of a 13 mm. human embryo 0·018 mm. in front of the point of entry of the hyaloid. *A*, margin of optic cup; *B*, the branches of the hyaloid artery in section.

These two parts are well developed by 16 mm. and can be seen, continuous with each other, in the eye shewn in Fig. 178. The mesoderm of the capsulo-pupillary vessels is continuous with the mesoderm which separates lens vesicle from surface ectoderm, there being as yet no anterior chamber. This mesoderm in front of the lens is not yet vascularised. It will be noted that at this stage the cavity of the optic cup is not large. Soon after this it begins to expand and at the same time short blind buds arise from the main trunk of the hyaloid artery. These extend and form branching vessels which completely fill the vitreous and anastomose freely with each other and with the vessels of the posterior portion of the tunica vasculosa lentis. These branches of the main trunk of the hyaloid in the vitreous are known as the *vasa hyaloidea propria*. They reach their maximum development about 40 mm. Fig. 179 shews them in the vitreous of embryos of 26 mm. and 35 and 48 mm. (in which the anterior or pupillary portion of the tunica vasculosa lentis is also apparent). They have thin walls, the mesodermal cells of which are in protoplasmic continuity with vitreous fibrils. At the height of their development they almost completely fill the optic cup, but in human embryos they never appear to come into direct contact with the retina.

In some other mammals (e.g. rodents) a certain number of them become applied to the inner surface of the retina, covering it with a vascular network

Digitized by Illinois College of Optometry Library

known as the *tunica vasculosa retinae*. From this tunica, in animals which possess it, the definitive retinal blood supply is developed, *but it must be noted that no trace of any such process occurs in man*. It is, however, possible, even in

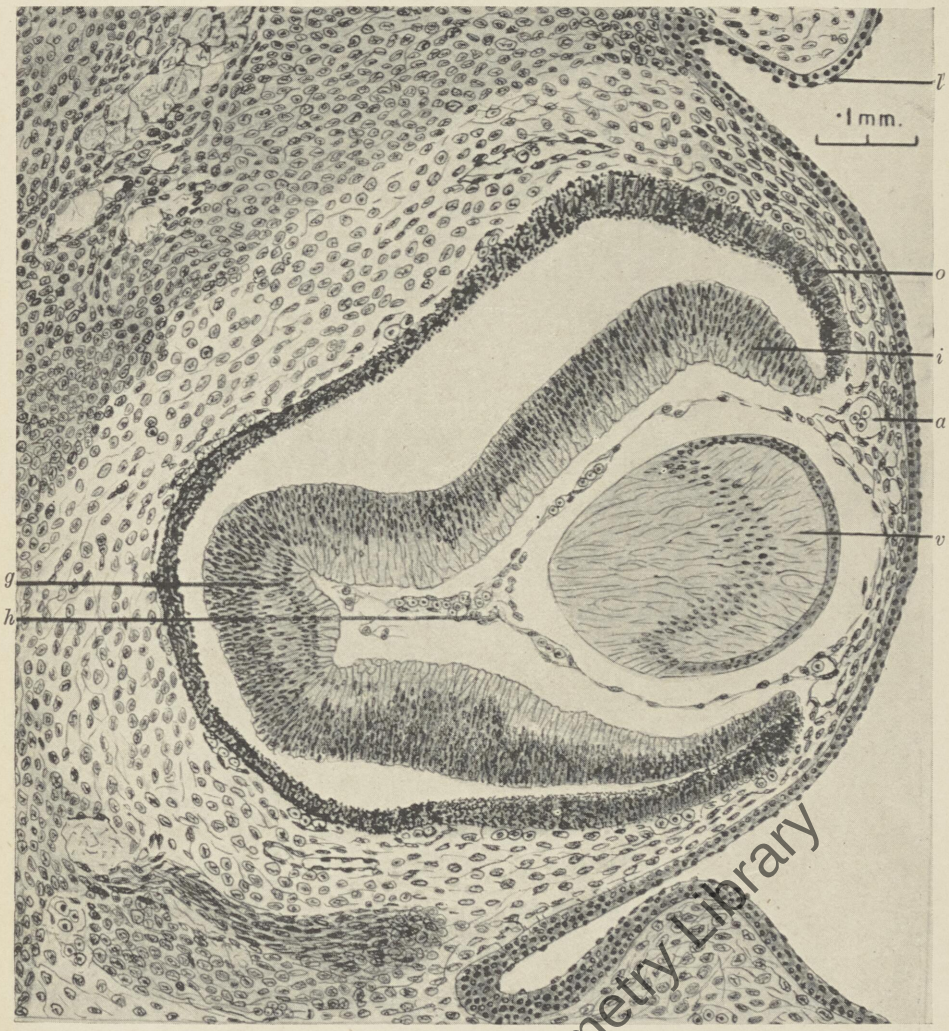
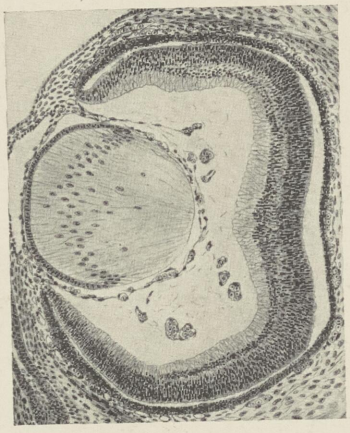


Fig. 178. Section through the eye of a 16 mm. human embryo. The annular vessel is seen in section at *a*. The lens (*v*) is surrounded by its vascular capsule formed by the branching of the hyaloid artery at *h*. Other points of interest in this section which should be noted are: *l*, the commencing lid fold covered with surface ectoderm which shews very clearly the divisions into epitrichial and nervous layers; *g*, the area of commencing differentiation of the inner layer (*i*) of the optic cup at the posterior pole: also the wide separation between the outer layer (*o*) and the inner layer of the cup and the absence of an anterior chamber.

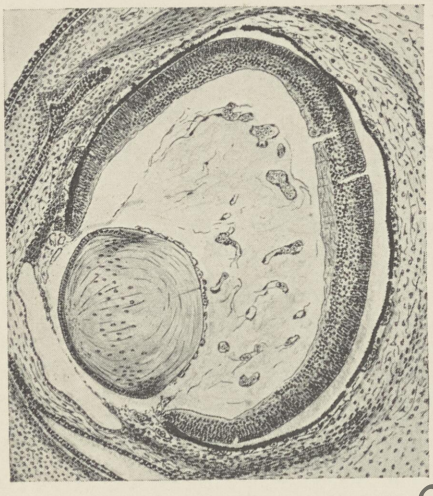
man, to divide the vitreous vessels into two sets, namely, an outermost set of small irregularly ramifying capillaries, and an inner set of slightly larger and straighter vessels surrounding the main trunk of the hyaloid. Morphologically the outer set probably represents the *tunica vasculosa retinae* of rodents.

Digitized by Illinois College of Optometry Library

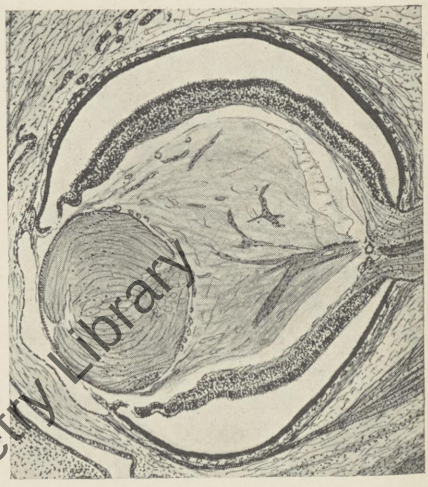
The condition of the intra-ocular vessels at 40 mm., at the height of the development of the vasa hyaloidea propria, is seen in the diagram Fig. 180. This extremely elaborate and rich vascularisation of the



A



B



C

Fig. 179. *A*, section through the eye of a 26 mm. human embryo. *B*, section through the eye of a 35 mm. human embryo. *C*, section through the eye of a 48 mm. human embryo.

interior of the eye and of the surface of the lens, which reaches its height at the beginning of the 3rd month of foetal life, is destined to disappear almost entirely before birth. Its *raison d'être* appears to be the supplying of nutriment to the developing lens, since in

Digitized by Illinois College of Optometry Library

man it is not concerned with the formation of the definitive retinal blood vessels. It is interesting, however, that it does not appear to be invariably necessary to the development of a lens, since among the Sauropsida we find the lens developing without any vascular capsule being formed at all. All the Mammalia shew this elaborate development of the hyaloid artery, though the details of its arrangement vary slightly in different species. In all it disappears practically

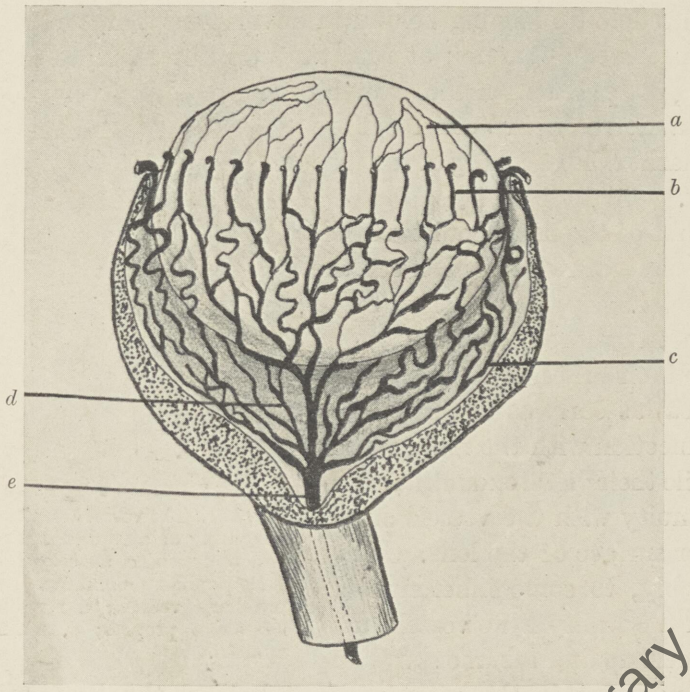


Fig. 180. Reconstruction of the hyaloid artery and its connections in a 40 mm. human embryo (after Versari). *a*, pupillary membrane; *b*, capsulo-pupillary vessels; *c*, outer set of vasa hyaloidea propria; *d*, inner set of vasa hyaloidea propria; *e*, main trunk of hyaloid artery.

completely, though at varying times, in some not until after birth. In man its retrogression begins towards the end of the 3rd month, and varies in rate in different parts.

From the 40 mm. stage onwards it becomes necessary to study each division of the tunica vasculosa lentis separately, since their fate is different. It is best to consider the posterior portion first.

The fate of the posterior portion of the tunica vasculosa lentis and the vitreous vessels. The posterior portion of the tunica vasculosa lentis is formed at first of a wide irregular meshwork of vessels occasionally widening into small blood lacunae. This netlike arrangement

Digitized by Illinois College of Optometry Library

never extends on the lens further forward than the equator, in front of which the vessels of the lateral or capsulo-pupillary portion of the vascular capsule always shew from the beginning a perfectly regular palisade-like arrangement without anastomoses. As the lens increases in size, the mesh of the posterior capsule becomes somewhat stretched, since the growth of the vessels does not keep pace with the growth of the lens, and in consequence the lacunae disappear and the calibre of the vessels becomes uniform. Soon after this stage (approx. 50 mm.) a definite lagging behind in development of the intra-ocular vessels becomes apparent; at first they do not increase in size and number *pari passû* with the growth of the eye, and very soon there sets in a decrease in actual calibre which marks the beginning of the true atrophy.

The first of the intra-ocular vessels to shew signs of retrogression are the vasa hyaloidea propria. They begin to shrink in calibre at their proximal ends (at their origin from the arteria hyaloidea) as early as 60 mm. They lose connection with the main vessels here while their distal ends still remain in continuity with the vessels on the posterior surface of the lens. Owing, presumably, to some inherent elasticity of the walls of the vessels, they tend to curl up and assume spiral and corkscrew forms in the vitreous, just behind the lens, after they have lost their connection with the main artery proximally. This leads to the condition seen in Fig. 181, in which the lens appears covered with curled vessels ending blindly in the vitreous. These are the vasa hyaloidea propria. The larger and more centrally placed of the vitreous vessels do not atrophy so early and can still be seen at 160 mm., though the smaller peripheral ones can no longer be recognised at this stage.

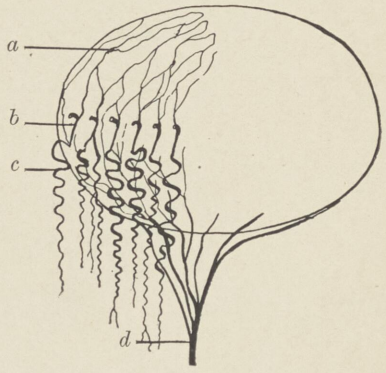


Fig. 181. The vessels on the lens at the beginning of atrophy of the vasa hyaloidea propria. *a*, anterior vascular capsule (pupillary membrane); *b*, capsulo-pupillary vessels; *c*, remains of vasa hyaloidea propria; *d*, main trunk of hyaloid.

The property of curling up of the atrophying vasa hyaloidea propria does not appear to be peculiar to them, as it is also shewn by the larger vessels in their turn and finally by the central trunk of the hyaloid artery itself. That this is the case can be easily verified by examination of living eyes, especially of children, by means of the slit-lamp, when the hyaloid remnant, of characteristic corkscrew form, can be seen in the majority of cases.

The atrophy of the vasa hyaloidea propria and of the more central set of vitreous branches (excluding the main trunk) is normally

Digitized by Illinois College of Optometry Library

practically complete by $8\frac{1}{2}$ months. A few small thread-like remnants of the larger ones usually persist throughout life forming the "muscae volitantes" often noticed by healthy eyes. They can often be seen floating in the vitreous near the back of the lens by means of the slit-lamp and, though not by any means invariable, must not be looked on as abnormal.

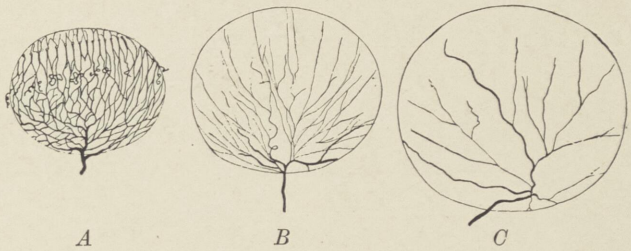


Fig. 182. Diagram shewing the retrogression of the posterior vascular capsule. *A*, at 85 mm. *B*, at 240 mm. *C*, at 280 mm. (after Versari).

The vessels on the back of the lens become progressively thinner and straighter and their point of origin from the hyaloid artery (i.e. its trifurcation) comes to be nearer and nearer the lens as this, increasing in diameter, stretches the atrophic vessels.

Fig. 182 shews stages in the disappearance of the posterior vascular capsule. The main trunk of the hyaloid narrows and finally becomes impervious in its central part towards the end of foetal life, probably during the 8th month. Atrophy proceeds more rapidly in its proximal than its distal portion as in the case of the other vessels in the vitreous, with the result that it loses its connection with the disc and floats free in Cloquet's canal from the back of the lens. Like the other vessels, its walls are elastic and it curls up into a corkscrew. This corkscrew shortens and withers still further, so that after birth it no longer remains extended in the line of Cloquet's canal but, under the action of gravity, comes to hang down behind the lens in a vertical direction. This may not occur until the 4th or 5th year.

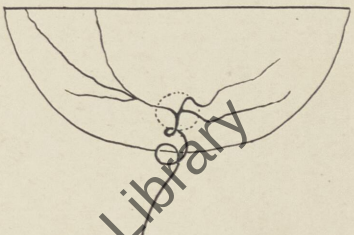


Fig. 183. Reconstruction of the lental end of the hyaloid artery during its retrogression.

Fig. 183 shews a reconstruction of the vessel on the back of the lens at a stage when, although still in connection with the optic disc, it is almost impervious to blood and is beginning to curl.

Digitized by Illinois College of Optometry Library

Fig. 184 shews the appearance seen with the slit-lamp in an eye at birth in which the vessel, though curled, is still pointing backwards in the line of Cloquet's canal.

Fig. 185 shews the appearance in the adult in which further shrinking has led to the remnant dropping down and hanging vertically. This represents the usual final stage of the atrophy, although in some individuals it may proceed further, and no trace of the hyaloid or any of its branches may remain in adult life.

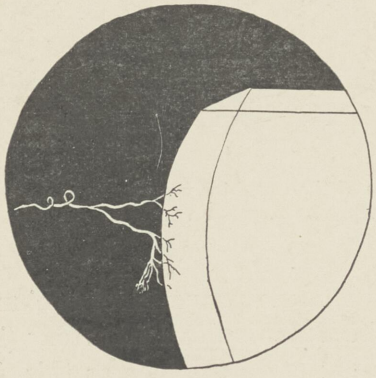


Fig. 184. Diagrammatic representation of the slit-lamp appearance of the hyaloid remnant at birth. The optical section of the lens is seen on the right; the hyaloid remnant stretches backwards into the vitreous on the left.

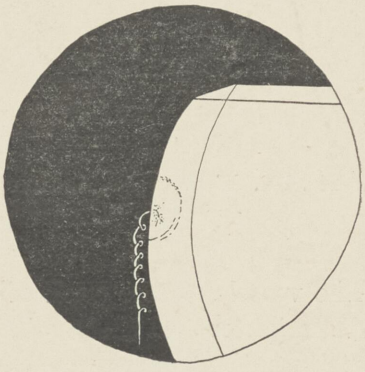


Fig. 185. Diagrammatic representation of the appearance of the hyaloid remnant as seen with the slit-lamp in the young adult. The optical section of the lens with the arc line on its posterior face is seen on the right. The hyaloid hangs down from this like a corkscrew in the so-called retro-lental space.

The fate of the lateral or capsulo-pupillary portion of the tunica vasculosa lentis. The vessels composing this are single, straight and unbranched. They can be seen at their best at any stage from 13–50 mm. (and traces of them can be discovered even as late as the 8th month, according to Versari). They run from the network of vessels forming the posterior portion of the tunica vasculosa lentis forwards between the equator of the lens and the ectodermal margin of the optic cup to drain into the annular vessel, and subsequently, when this has become unrecognisable as a definite vessel, into the most anterior loops of the choroidal net. The flow of blood in them is from behind forwards.

It is obvious from Fig. 186 that their connection with the annular vessel is only easy and free during the time before the forward growth of the ectodermal margin of the optic cup beyond the equator of the lens (i.e. before the 50 mm. stage). When this begins to occur it will naturally tend to cut across the line of vessels and stretch them

Digitized by Illinois College of Optometry Library

forward, so that in order to reach the annular vessel they must take a sharp lateral bend after escaping beyond the margin of the growing

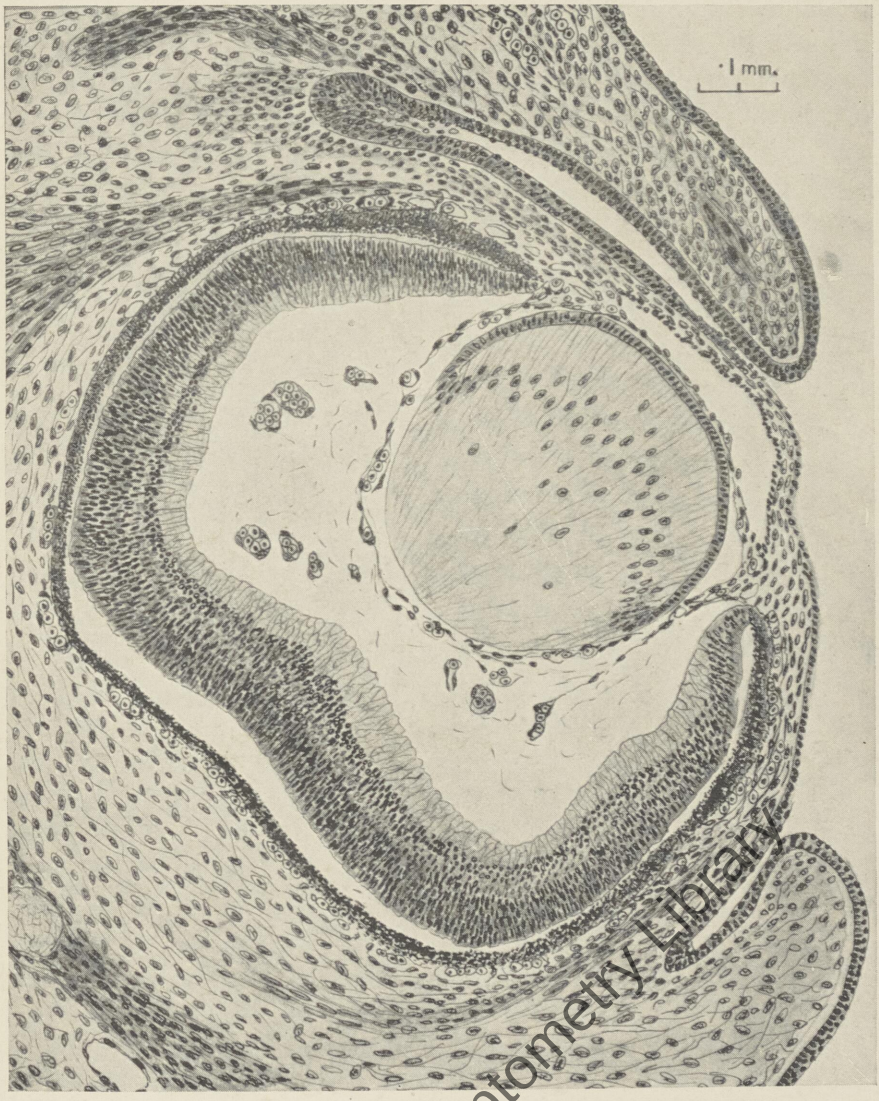


Fig. 186. Section through the eye of a 26 mm. human embryo. Note the vasa hyaloidea propria in the vitreous and the vessels in contact with the lens capsule and around the opening of the cup.

cup. This stretching, kinking and pressure soon leads to their atrophy, occurring, as it does, at a time (50 mm.) when, owing to the atrophy of the vasa hyaloidea propria, the blood reaching the back of the lens is already considerably less than formerly. The period of forward

Digitized by Illinois College of Optometry Library

growth of the margin of the cup to form the ectodermal layers of the iris is therefore also the period of atrophy of the capsulo-pupillary vessels (or irido-hyaloid, as they are occasionally called). The vessels shrink and disappear first at the growing edge of the ectodermal iris. They can long be recognised running as far as this (Fig. 187), but cease to be visible turning over the edge during the 4th month. Their disappearance allows of the development of the definitive structures in the equatorial region of the lens, i.e. the suspensory ligament and the ciliary processes. Their function, the draining of

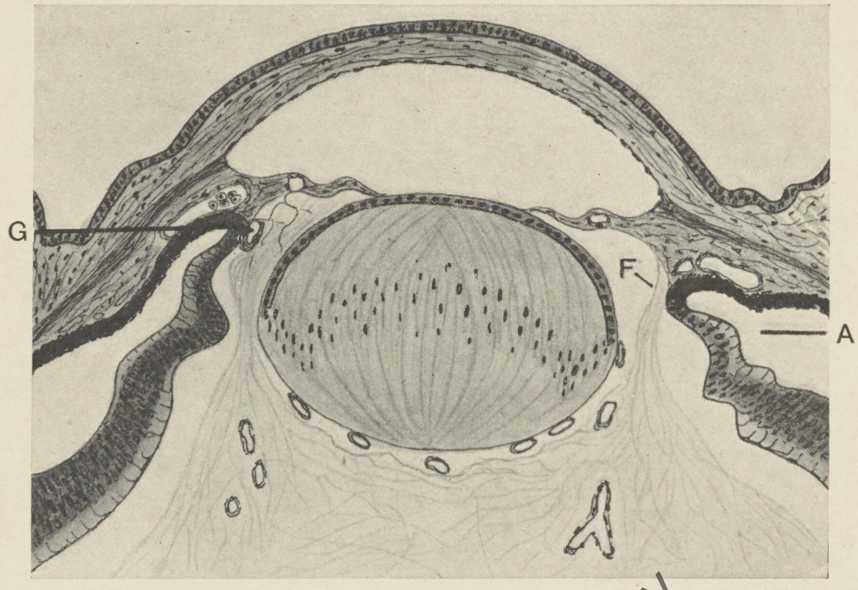


Fig. 187. Section through the anterior part of the eye of a 25 mm. human embryo. *A*, remains of cavity of primary optic vesicle; *F*, "faisceau isthmique" of vitreous (see p. 179); *G*, remains of capsulo-pupillary vessel.

blood from the hyaloid artery into the choroid, ceases to be essential with the onset of atrophy in the branches of the hyaloid, and this latter may possibly be in part precipitated by the lessening calibre of the drainage channel by stretching.

The fate of the anterior or pupillary portion of the tunica vasculosa lentis, together with the differentiation of the mesodermal portion of the iris and the formation of the anterior chamber. As we have seen, at 16 mm. (Fig. 178) the anterior surface of the lens is in contact with a thin layer of mesoderm which separates it from the surface ectoderm. This layer is only a few cells thick and contains no blood vessels except at its periphery, where a few blind buds from the

Digitized by Illinois College of Optometry Library

annular vessel are extending into it. Soon after this stage a split (formed apparently by the coalescence of vacuoles in its deeper part) occurs, separating it into two layers, an anterior slightly thicker and more densely arranged, in contact with the posterior surface of the surface ectoderm, and a posterior, extremely tenuous and in contact with the anterior surface of the lens. The space between the two layers is at first very narrow. It can just be recognised at 18 mm. and is easily seen at 22 mm. It is the rudiment of the anterior chamber, but is at first a completely closed space bounded everywhere by mesoderm. The mesoderm of its anterior wall is completely avascular from the beginning, but that of its posterior wall becomes rapidly vascularised by the extension of the buds of the annular vessel noted above into it (20–25 mm.). Very soon the mesoderm cells immediately bounding this closed anterior chamber become regularly arranged to form an endothelial lining for it. This endothelium is always more marked on the anterior (or corneal) wall than on the posterior. This condition of the anterior chamber can be seen in Fig. 186, which shews an eye of a 26 mm. human embryo. The anterior chamber, bounded in front by the corneal mesoderm and behind by the mesoderm of the anterior vascular capsule of the lens, can be seen as a wide space. The continuity of the mesoderm in front of the lens with the capsulo-pupillary and posterior portions of the tunica vasculosa lentis is obvious. At this stage the annular vessel can still be seen at the margin of the optic cup, and the vessels both of the anterior and the capsulo-pupillary portion of the tunica drain into it.

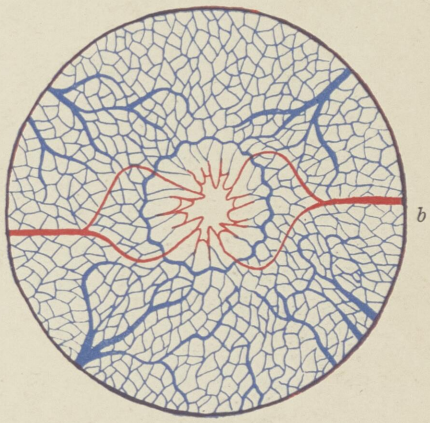


Fig. 188. The anterior portion of the choroid and pupillary membrane at the 25 mm. stage, after the appearance of the long ciliary arteries but before their anastomosis. The annular vessel is seen in the centre and the long ciliary arteries at *b*, *b*. The large radial veins are tributaries of the venae vorticosae.

At this stage the appearance of the anterior portion of the tunica vasculosa lentis seen from the front in an injected specimen is that seen in Fig. 188. Now that the anterior chamber has formed, this anterior portion can be designated as the *pupillary membrane*.

The "pupil" at this stage, of course, is slightly wider than the equator of the lens, as the ectodermal iris has not yet appeared. The pupillary membrane is therefore the whole of the mesodermal layer stretching across the

Digitized by Illinois College of Optometry Library

opening of the optic cup. It includes at this stage therefore a portion of mesoderm which will eventually be backed by the ectodermal iris as this grows forwards, and will then form part of the mesodermal iris stroma.

Even at 25 mm. it is apparent that the pupillary membrane can be divided into two regions, a *peripheral* and a *central*. The peripheral region, which is in continuity with the lateral portion of the tunica vasculosa lentis, is much thicker and richer in cells than the central, which is an extremely diaphanous membrane, almost acellular except

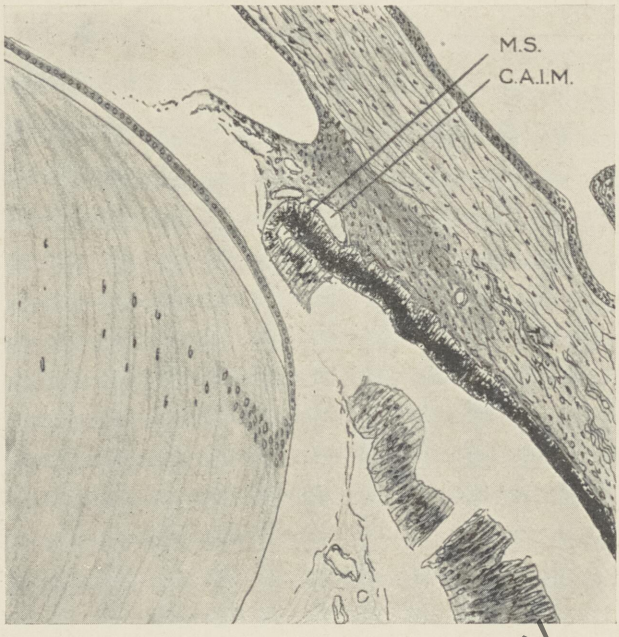


Fig. 189. Section through the margin of the optic cup of a 25 mm. human embryo. *M.S.*, marginal sinus; *C.A.I.M.*, circular anteriorus iridis major.

in the neighbourhood of the vessels. This central portion is destined to disappear completely, while the lateral portion persists. The first change in the pupillary membrane occurs at about 48 mm. when its peripheral portion begins to lose connection with the capsulo-pupillary vessels owing to forward growth of the margin of the optic cup. Soon after this the relations are those shewn in Fig. 189, in which a short thick ectodermal iris is appearing, growing forward deep to the mesoderm of the pupillary membrane, which is now even thicker in its peripheral part. The angle of the anterior chamber is wide open and quite obvious, although the ciliary region is as yet undifferentiated.

It is obvious that at this stage (since the ciliary body is incomplete) the fluid presumably filling the anterior chamber is not to be regarded as aqueous,

Digitized by Illinois College of Optometry Library

but merely as a liquid comparable with that filling other cavities in the embryo at this stage (e.g. the central nervous system). It does not appear to acquire the distinctive characters of aqueous humor until after the development of the ciliary glands at the 110 mm. stage (beginning of 5th month), and until that time is very small in amount. In many specimens, even up to the 6th month, the anterior chamber appears empty, extremely narrow and compressed. Its early anatomical differentiation is not correlated with an early function but rather the reverse, it being shallower even at birth than it is in the adult.

As the ectodermal iris grows forward the mesoderm in contact with it thickens, becomes still more vascular and can be arbitrarily divided into two or more layers of vessels. The central part, however, remains thin, but the loops formed by the vessels in it extend by throwing out further buds, so that a series of loops arranged in arcades begins to be formed. This process reaches its height during the 5th month, when the membrane is supplied by three and in places four tiers of arcades. The appearance of the membrane at this stage is seen in Fig. 190. Only three-quarters of the membrane are shewn, the fourth having been torn during preparation. The ectodermal iris (with the paler sphincter forming a band at its pupillary edge) is seen lying deep to the membrane. The pupil appears dilated, since growth of the ectodermal portion is incomplete as yet. During this period of ectodermal growth and vascular extension in the iris region, the peripheral part of the pupillary membrane has continued to thicken, and sets of deeper vessels are making their appearance in it, giving rise to the rete of the iris stroma. These vessels are an ingrowth of small branches of the long ciliary arteries into the peripheral portion of the pupillary membrane. These arteries now give off three main sets of branches, the most superficial supplying the large vessels of the arcades of the pupillary membrane, the next passing to the iris stroma and the third, recurrent, turning back towards the ciliary region. These vessels of the rete extend from the periphery *pari passû* with the extending ectodermal iris and, when the sphincter pupillae differentiates from this, small capillary branches from them invade it, carrying mesoderm with them. By this means it becomes broken up by connective tissue septa into separate muscle bundles, which are vascularised by two plexuses derived from these branches of the long ciliary arteries, namely an *inter-sphincteric* plexus in the substance of the muscle and a *sub-sphincteric* plexus lying between it and the pigmented epithelium from which it was derived. This process is more or less completed during the 7th month so that, at the end of this, four layers of vessels can be recognised in the peripheral portion of the pupillary membrane (now to be called the iris stroma).

Digitized by Illinois College of Optometry Library

These layers are as shewn in Fig. 191:

1. The most *superficial*, composed of large arteries and veins directly continuous with each other in the central portion of the pupillary membrane and forming the vascular arcades of this.

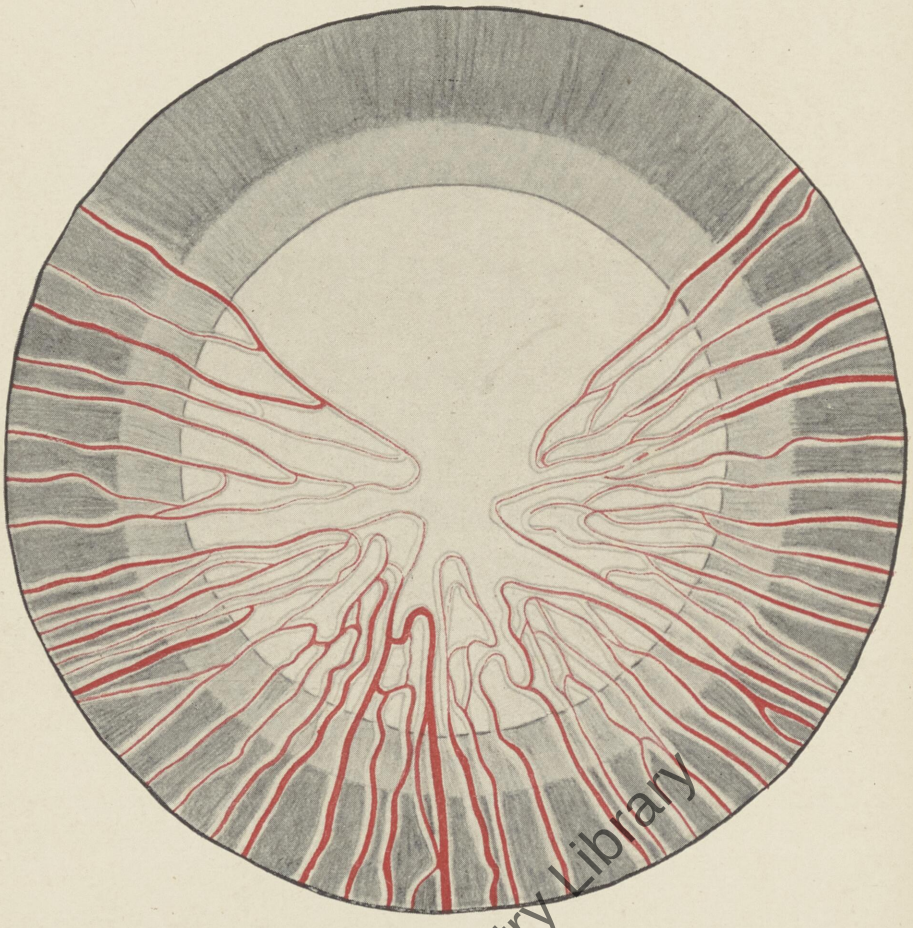


Fig. 190. Appearance of the pupillary membrane of a 5 months human foetus seen from the front. The specimen was drawn with the aid of a Gullstrand slit-lamp after removal of the cornea. The colour of the blood can be easily seen through the vessel wall in the actual specimen and is not diagrammatic.

2. A *deeper* set of veins and arteries vascularising the iris stroma.

3. A plexus of capillaries (*inter-sphincteric*) in the substance of the sphincter pupillae.

4. A plexus of capillaries (*sub-sphincteric*) lying between the sphincter pupillae and the pigment epithelium of the iris. They can be seen in section in Fig. 191.

During the 7th month, while the vascularisation of the meso-

Digitized by Illinois College of Optometry Library

dermal portion of the iris is attaining its definitive condition, the process of atrophy which has already declared itself in the posterior and lateral portions of the tunica vasculosa lentis begins to involve the anterior portion of this also. The fact that atrophy of the pupillary membrane is delayed in this way is correlated on the one hand with its later development (the buds from the annular vessel do not appear until the posterior and lateral portions are complete) and on the other with the development of secondary channels of supply from the long ciliary arteries outside the cup, whereas the rest of the tunica vasculosa lentis depends solely on the arteria hyaloidea. The atrophy of the pupillary membrane affects only the central part, which was

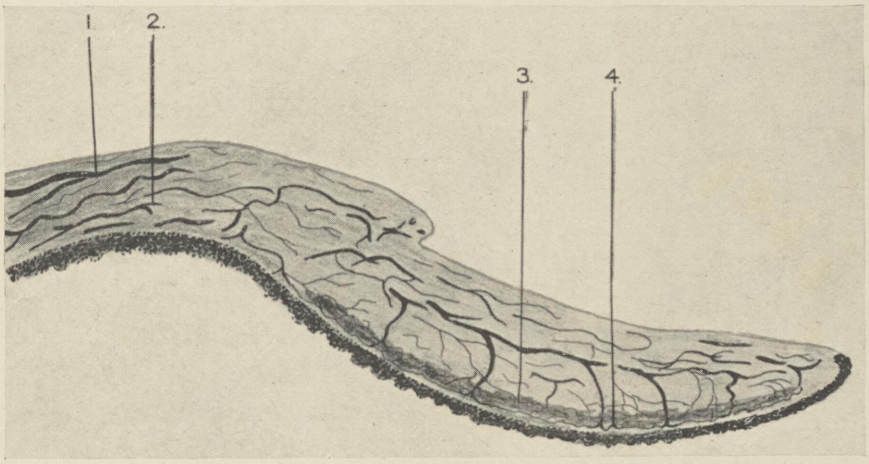


Fig. 191. Section (after Versari) through the iris, to shew the four sets of vessels described in the text, in a foetus at term.

noted to be thinner than the periphery from the beginning. It consists of a gradual shrinkage of the walls of the vessels with lessening of the lumen and final cessation of the blood flow. It first affects the loops of the final arcades in the centre of the membrane, so that the circulation is carried on by the next relay of arcades peripherally. The central loops which are out of action simply shrink; they do not break away and assume spiral forms as do the vasa hyaloidea propria on the back of the lens.

The commencing atrophy of the central loops is seen in Fig. 192, which shews the iris of a 7 months foetus from the front. Three tiers of arcades can still be traced in the pupillary membrane, but the contrast between the central portion comprising the thin second and third arcades and the peripheral portion with its dilated first series of anastomotic loops is striking. The ectodermal portion of the iris,

Digitized by Illinois College of Optometry Library

carrying with it to its margin the mesodermal layer of capillary plexuses in connection with the sphincter has increased considerably in width since the stage seen in Fig. 190. It now comes to lie deep to a portion of the second arcade of the pupillary membrane. As the atrophy of this second arcade proceeds it becomes separated from the underlying pupillary margin, and an appearance as of two layers, an anterior (the pupillary membrane) and a posterior, the

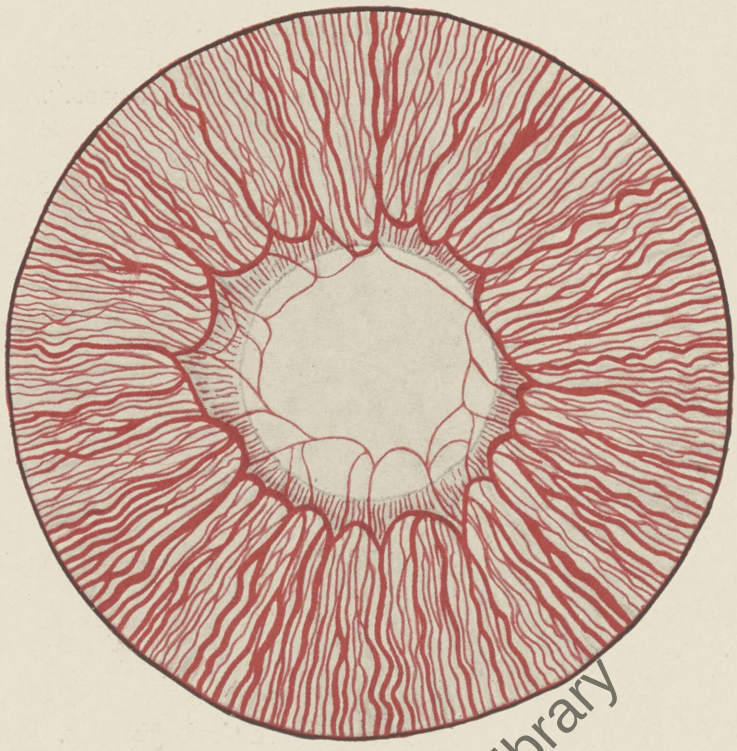


Fig. 192. Appearance of the iris and pupillary membrane of a 7 months human foetus seen from the front. The specimen was prepared and drawn in the same way as that shewn in Fig. 190.

margin of the true pupil with its vessels, is produced, with a chink or cleft between them. (The appearance of the pupil margin before and after the commencement of atrophy is seen in Figs. 193 and 194 shewing sections of this region at 5 and 7 months.) This chink (sometimes called *Fuchs' cleft*) is of very variable extent. In some cases it can only be found at the pupil margin. In others it undermines the superficial layer of vessels peripherally for a considerable distance. In rare cases, probably pathological, the process of atrophy which produces it is not arrested in infancy but continues slowly throughout life, so that finally the whole of the superficial

Digitized by Illinois College of Optometry Library

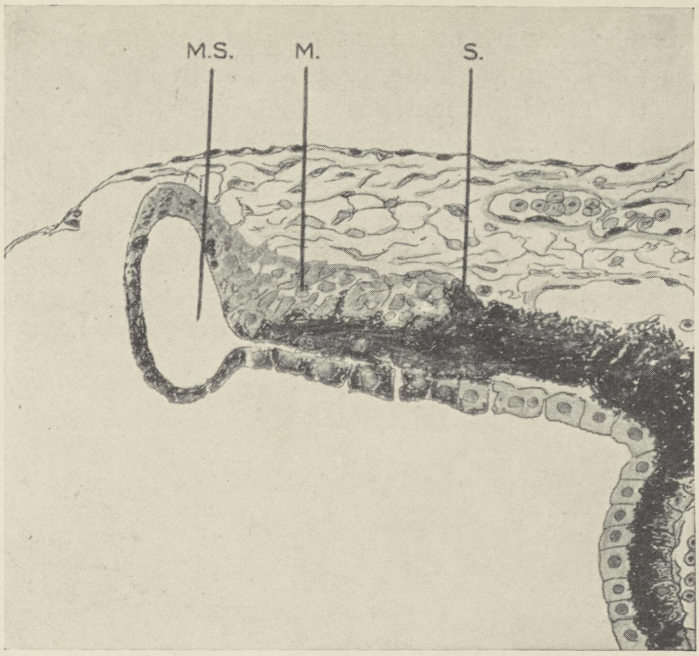


Fig. 193. Section through the iris of a human foetus of 5 months (150 mm. approx.). *M.S.*, marginal sinus; *M.*, sphincter pupillae; *S.*, Michel's spur.

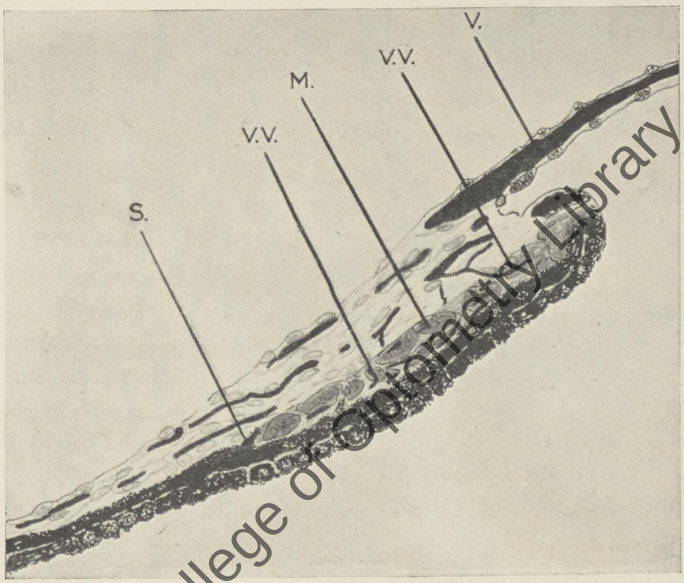


Fig. 194. Section through the iris of a 7 months human foetus (230 mm. approx.). *S.*, Michel's spur; *V.V.*, small vessels penetrating the sphincter mass *M*; *V.*, large superficial vessel of the pupillary membrane.

Digitized by Illinois College of Optometry Library

layer of vessels of the iris becomes separated from the deeper portion and floats loosely in the anterior chamber in front of the main portion of the iris, to which it is attached at the periphery only. Localised patches of atrophy also frequently occur in the superficial layer peripheral to the pupil margin and give rise to the appearance

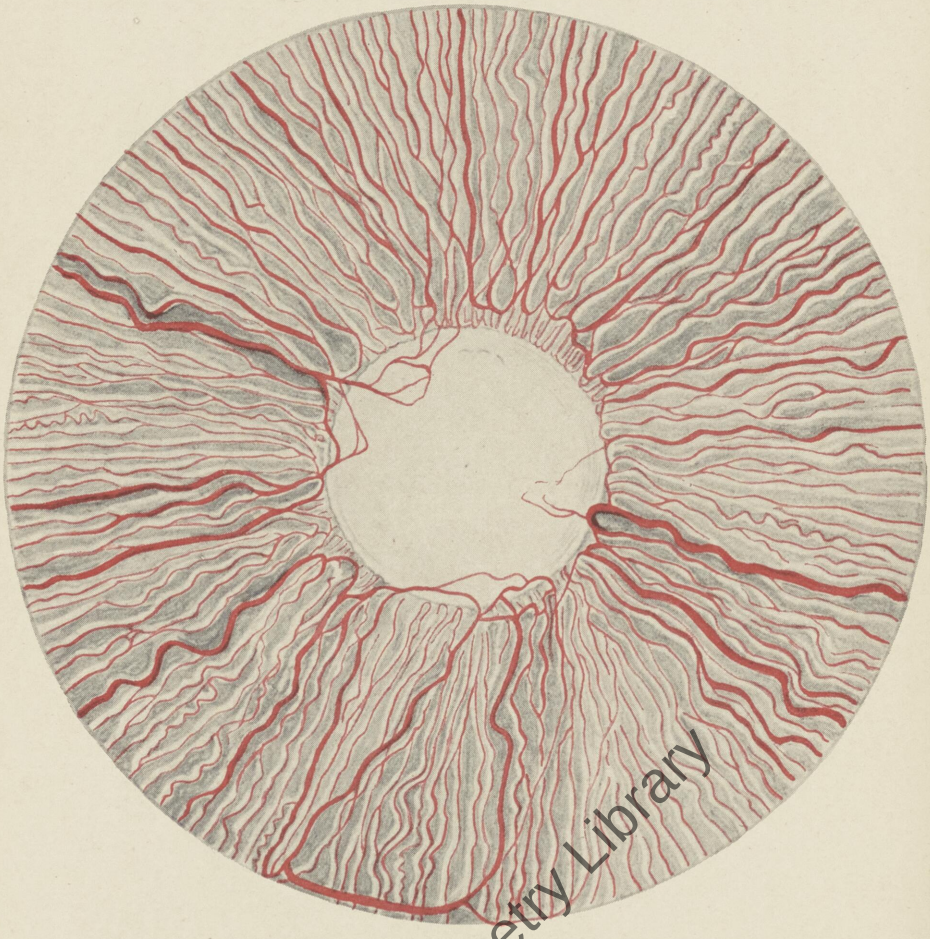


Fig. 195. Appearance of the iris and remains of the pupillary membrane of a human foetus of 8½ months. Preparation similar to that of specimens in Figs. 190 and 192.

of deep crypts in the iris stroma. The final patterning of the adult iris is subject to an infinity of variations, depending primarily on the amount of atrophy and secondarily on the amount of subsequent pigmentation.

The atrophy of the pupillary loops continues, the blood returning more and more by the first anastomotic arcade, which even at 7 months can be recognised as the future "lesser circle" of the iris.

Digitized by Illinois College of Optometry Library

It is thus clear, as has so often been pointed out by anatomists, that the lesser circle is not an arterial circle but an arterio-venous anasto-

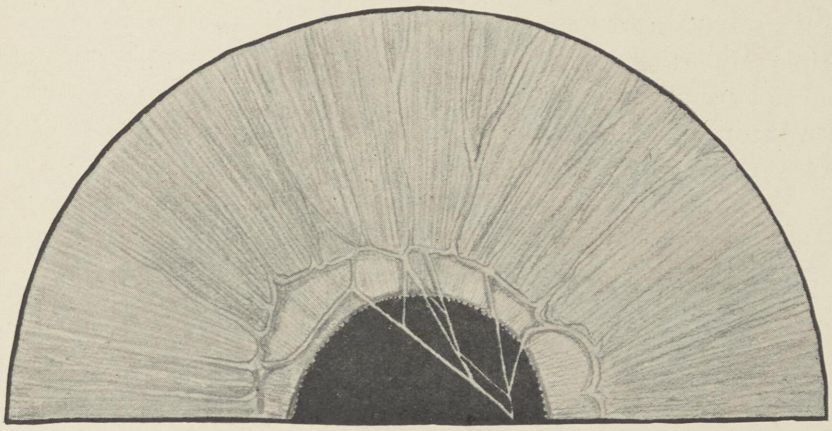


Fig. 196. Half the iris of a full term human foetus shewing remains of pupillary membrane coming from the lesser circle. No blood was visible in this specimen, shewing that the vessel walls have thickened since the last stage.

mosis. Its old name, "circulus *arteriosus* iridis minor," should therefore be abandoned in favour of the more suitable one, "circulus *vasculosus* iridis minor."

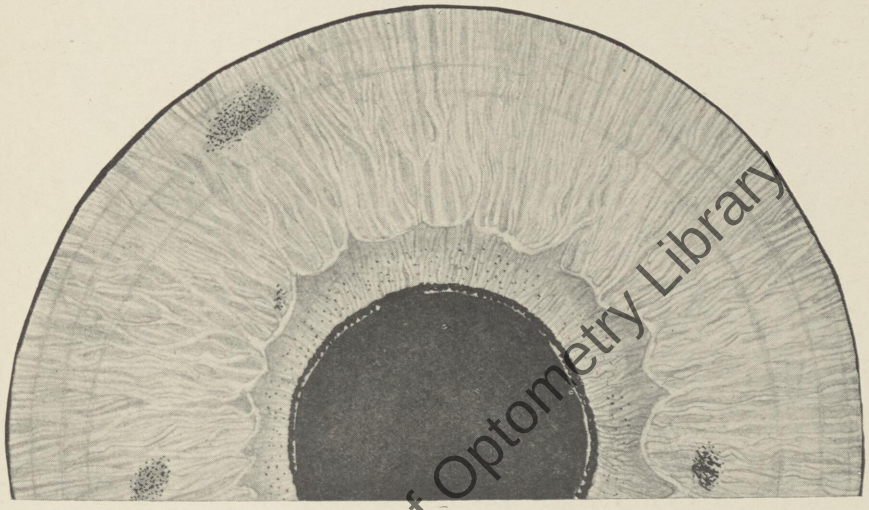


Fig. 197. Portion of the iris of a man of 65.

By $8\frac{1}{2}$ months (Fig. 196) most of the central loops of the pupillary membrane have atrophied and the lesser circle is established as the sole channel of return of the blood reaching the central portion of the iris by way of the superficial vessels of the stroma.

Digitized by Illinois College of Optometry Library

In places the remnants of the first and second arcades still contain blood. The vessels of the iris stroma have increased in number and complexity. Since the persistence of the third arcade as the lesser circle provides a free channel for the circulation of the blood in the peripheral portion of the pupillary membrane, this peripheral portion does not usually undergo any atrophy, but its vessels continue to form throughout life the large thick-walled superficial vessels of the

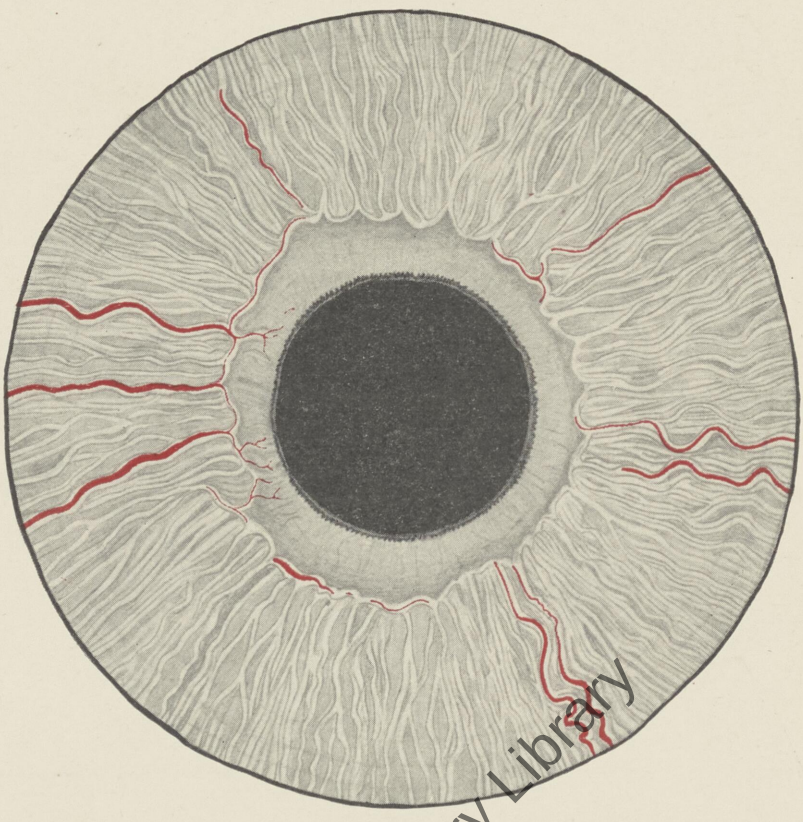


Fig. 198. The iris of a man of 31 with early acute iritis. The blood column has again become visible in some of the vessels.

iris. The exact amount of atrophy of this superficial layer varies very considerably in the individual. In Fig. 196 is shewn a portion of the iris of a full term foetus with the superficial layer of the iris complete up to the lesser circle, from which come fine strands (without any circulating blood) representing a few persisting remains of the central loops of the membrane in Fig. 190. In Fig. 197 a portion of the iris of a man of 65 years of age is seen, in which the condition is similar, only without any strands coming from the lesser circle. In Fig. 198 is shewn the iris of a man of 31 with commencing acute

Digitized by Illinois College of Optometry Library

iritis. The inflammation has led to the dilatation of the larger vessels of the stroma and of the lesser circle, so that the blood column is once more visible within them. The arrangement of vessels should be compared with the foetal condition in the preceding figures. From Fig. 197 it can easily be seen why, in cases of persistent pupillary membrane in the adult, the tags of tissue are always attached to the region of the lesser circle and not to the pupil edge. They represent, of course, remnants of the second and third tiers of arcades which drained into the superficial vessels here.

The *development of pigment in the stroma of the iris* occurs after birth and to a very variable extent. In Fig. 197 are seen three small patches of pigment anterior to the vessels. In deeply pigmented eyes an extensive deposit takes place in the superficial layer, so that the details of structure may be entirely hidden. It must be realised that the so-called "sculpturing" of the iris seen in life in blue and grey eyes is due to the visibility of the vessel walls and, occasionally under magnification, of the blood column itself, the intervening stroma being quite transparent. In brown eyes the stroma is no longer transparent and the vessels cannot be seen, except those which may be in relief on the surface. In light blue eyes during life, with good illumination and magnification (of twenty-four or more), it is often possible actually to make out two or sometimes three layers of vessels which may cross at acute angles, the deeper ones running to the pupillary margin, the superficial ones anastomosing at the lesser circle.

The differentiation of the vessels of the ciliary body. Towards the middle of the 4th month, when the ectodermal folds of the future ciliary processes are already present, the beginnings of the ciliary vessels can be recognised. The anterior portion of the choroidal net now shews a parallel arrangement of the larger vessels, which run a more or less straight course forwards towards the iris region, where they again form a net. Most of these vessels are veins. As they pass forwards and run beneath the ciliary folds, those corresponding to the summit of a fold become raised up, enter the fold, run along its highest part and join the general net again in front of it. They are connected during their passage along the fold by numerous small branches with the vessels external to them, so that the vessel in the process has rather the appearance of a little comb with teeth directed out towards the choroid. This arrangement is seen in Fig. 199 which shews the region in an injected specimen. The long ciliary artery bifurcating and beginning to form the major circle of the iris is also

Digitized by Illinois College of Optometry Library

seen. It gives small branches to the iris and the pupillary membrane but the vessels of the ciliary processes are as yet entirely venous in nature. This condition continues, with increase in size of the tufts of veins in the ciliary processes, so that they now have a "head," rounded and directed anteriorly, and a "tail," flattened and merging into the choroid behind. At the beginning of the 6th month (210 mm.) the appearance of the ciliary processes is that seen in Fig. 200. The major circle is complete at this stage and three sets of branches from it are recognisable.

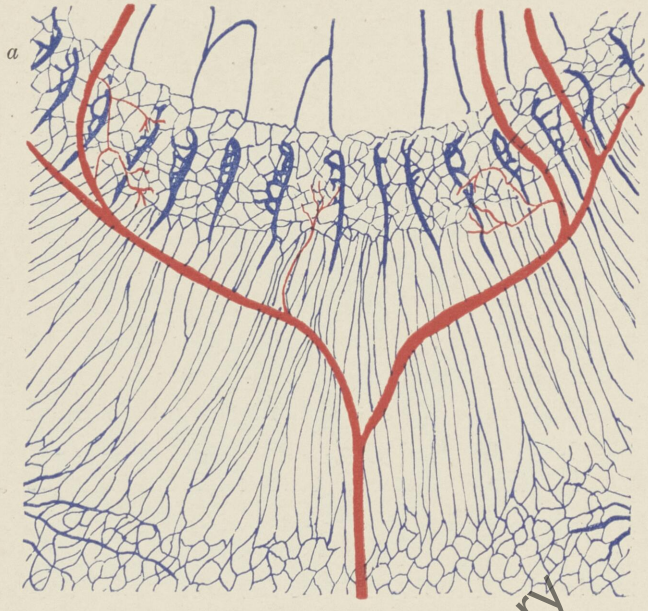


Fig. 199. The arrangement of the vessels in the ciliary region in a 110 mm. foetus (after Versari). The commencing ciliary veins are seen in blue at *a*, a long ciliary artery and its branches is shewn in red.

1. Large superficial vessels of the pupillary membrane.
2. Small vessels to the iris stroma.
3. Recurrent vessels to the ciliary region.

These last are small at this stage, but they gradually extend, and one reaches each ciliary process and vascularises it at the end of the 8th month. Fig. 201 shews the ciliary and iridic vessels during the 3rd week of the 8th month. Little change beyond increase in size of the arteries to the ciliary processes and further atrophy of the branches to the pupillary membrane occurs after this.

Digitized by Illinois College of Optometry Library

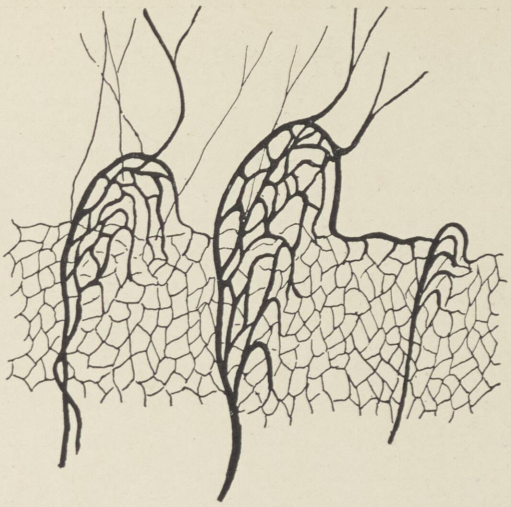


Fig. 200. The vessels in three ciliary processes of a 210 mm. foetus (after Versari).

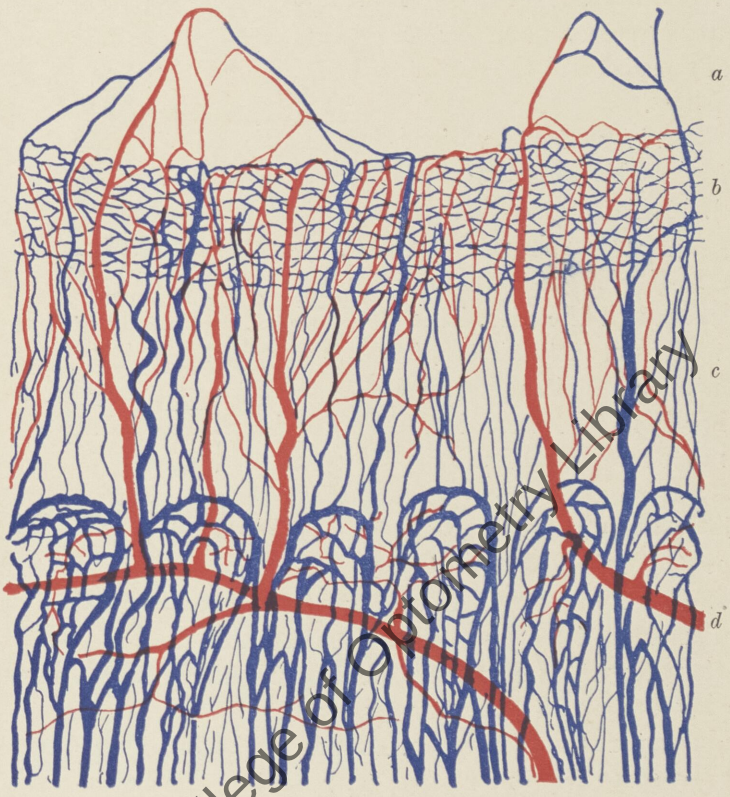


Fig. 201. The injected vessels of the iris and ciliary region (after Versari) in a 290 mm. human foetus. *a*, zone of pupillary membrane loops; *b*, zone of sphincter pupillae with its plexuses; *c*, radial vessels, arteries and veins of iris stroma; *d*, ciliary processes and main branches of the major circle.

Digitized by Illinois College of Optometry Library

4. The Development of the Definitive Retinal Arteries and Veins

The retina and the optic nerve are, as we have seen, during the first period of their development completely avascular. The hyaloid artery enters the optic stalk, it is true, at an early age, but it gives no branches to it, and merely runs through it to reach the cavity of the optic cup. There is at first no accompanying vein with the hyaloid artery. This does not begin to appear until during the 3rd month, when there are recognisable on either side of the artery two other blood channels. These run through the nerve parallel with the artery and are united to each other by numerous anastomoses. As they pass backwards from the ocular end of the nerve they approach each other, and finally coalesce at a variable distance behind the disc, forming thereby the main trunk of the *vena centralis retinae*. Tributaries of them can thereafter be seen among the nerve fibres of the disc and the distal end of the nerve.

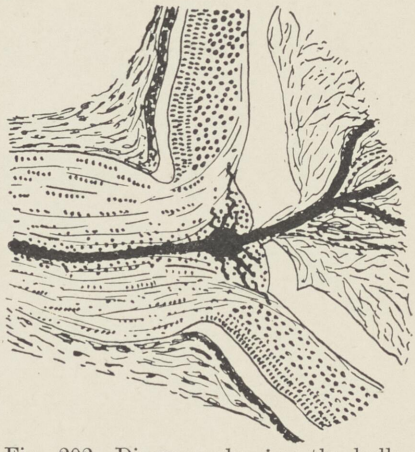


Fig. 202. Diagram shewing the bulb of the hyaloid artery and its branching on the disc to form the arteria centralis retinae.

The *arteria centralis retinae* is just recognisable at 100 mm. (4th month). At this time a small bulbous swelling appears on the trunk of the arteria hyaloidea just where it is passing through the disc. This enlarges and from it two small buds grow out, one from its upper aspect, the other from its lower. These are the beginnings of the upper and lower main branches of the arteria centralis retinae. Other arterial twigs arise from these and from the bulb of the main artery, and ramify in the little cone-shaped mass of cells (Bergmeister's pupilla, see p. 109) in the centre of the disc. This is shewn in a semi-diagrammatic manner in Fig. 202. From within this cone, which enlarges and surrounds the hyaloid artery as it enters the vitreous, forming its glial sheath, these capillaries grow out and ramify in the substance of the nerve fibre layer. By 4 months they have vascularised a small area of the nerve fibre layer around the disc. Thence they spread peripherally and also at the same time more deeply, reaching finally the ora serrata and the inner nuclear layer. They do not reach the ora serrata till 8 months, at which time their development is complete. Their accompanying veins, tributaries of the vena centralis retinae, appear

Digitized by Illinois College of Optometry Library

as small capillary channels coincidentally with them. These channels open finally by two main trunks on the disc into the two accompanying veins of the arteria centralis retinae within the first part of the nerve.

The bulb-shaped swelling on the hyaloid artery, from which the retinal arteries develop, marks the point back to which the main trunk of the hyaloid will eventually atrophy. Before this happens, however, the proximal part of the hyaloid in the vitreous appears to undergo a further specialisation after the appearance of the bulb. Its walls thicken somewhat and the glial cells of Bergmeister's papilla, around its point of exit from the disc, proliferate and grow out into the vitreous along it. They form a sheath for it which is in form a cylindrical tube through which the first part of the artery runs. The walls of this tube are not in intimate contact with the walls of the artery, which run free within it, but they are united to the artery by numerous fine threads of protoplasm in much the same way as the cells of the artery wall are at any earlier stage united to the ectodermal fibrils of the vitreous along the boundary of Cloquet's canal. This tube surrounding the proximal portion of the hyaloid is known as its *glial sheath*. It is ectodermal in nature. It reaches the height of its development at about 180 mm., when it extends along the first one-third of the artery. This can be seen in Fig. 148 *C* and *D* which shews it in a diagrammatic reconstruction, while its appearance on section is that in Fig. 203 *a*. Fig. 203 *b* shews Bergmeister's papilla in a 32 mm. human embryo. The cells which proliferate to form the glial sheath can be seen on either side of the hyaloid artery.

During the 7th month it begins to atrophy, this change extending in most cases even below the surface of the disc, so that finally a slight excavation, the physiological pit, is produced at the site of the former prominence. The hyaloid artery itself shrinks *pari passû* with it, though not quite so rapidly.

This transient glial protuberance from the centre of the disc in man is of interest morphologically as it is in many ways reminiscent of the vascular ectodermal projections found in the eyes of Sauropsida (i.e. various forms of pecten). Whether or not the two can be truly homologised is doubtful, though it is certain that both form as ectodermal outgrowths from the wall of the optic cup vascularised by the hyaloid artery or derivatives of it. In those animals in which it persists a true retinal blood supply never develops. In man it disappears with the establishment of the permanent retinal circulation.

The various degrees of so-called fibrous tissue on the disc and of excessive shallowness or depth of the physiological pit are all probably correlated with the degree of persistence or atrophy of this glial sheath at its origin from the disc.

Digitized by Illinois College of Optometry Library

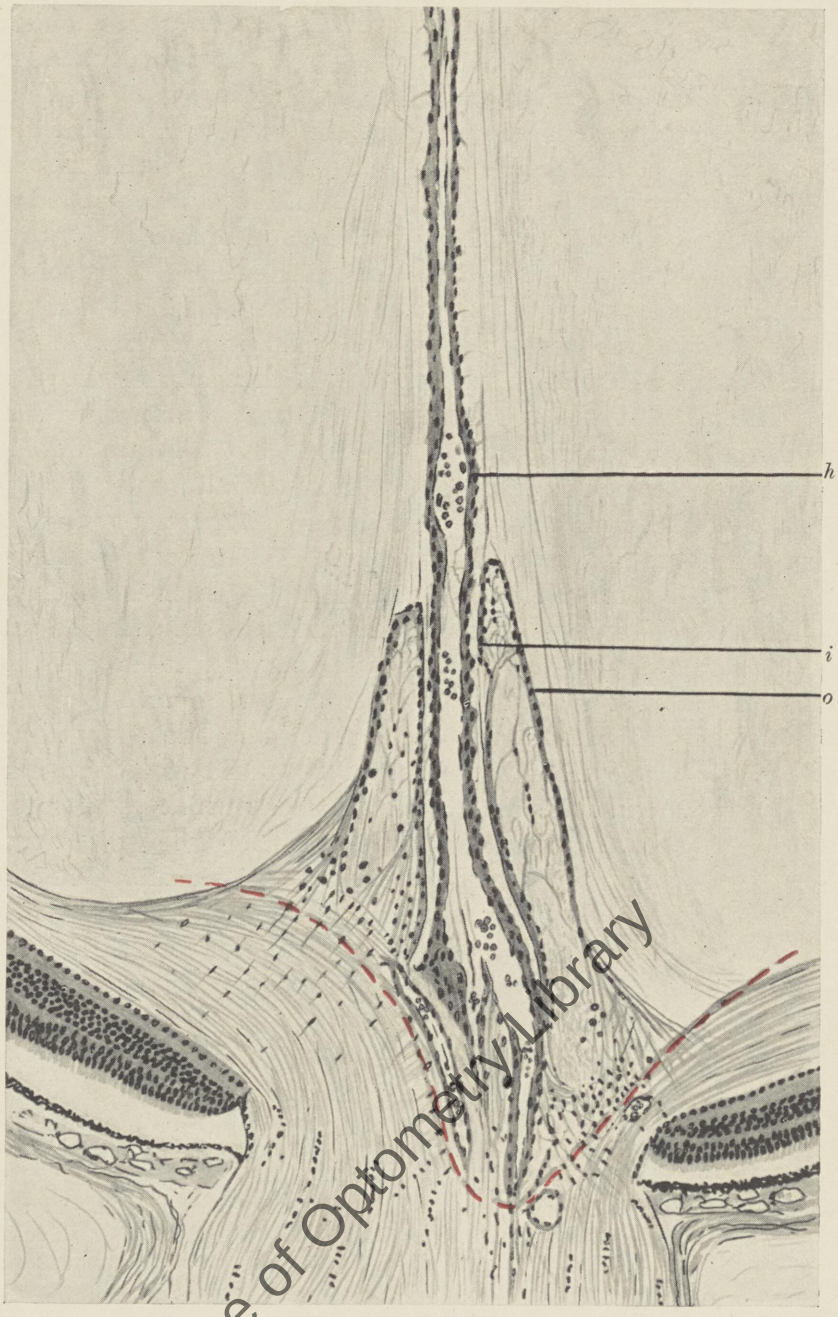


Fig. 203 *a*. Section (after Bach and Seefelder) of the glial sheath of the hyaloid artery at 180 mm. *h*, wall of hyaloid artery; *i*, inner and *o*, outer layer of glial sheath. The red line represents the limit of final atrophy and therefore the level of the physiological pit.

Digitized by Illinois College of Optometry Library

The **vessels of the optic nerve** come from two sources and at different times. Those of the portion *distal* to the point of entry of the arteria hyaloidea are derived from small capillary off-shoots from this which run between the bundles of nerve fibres. Drainage is into the vena centralis retinae. Those of the *proximal* portion of the nerve appear earlier (65 mm.) near the brain at first, and spread rapidly forwards. They are small channels derived from vessels lying around the nerve in its mesodermal sheath. They invade the nerve (65–73 mm.) carrying with them connective tissue which helps to separate the nerve fibres into bundles.

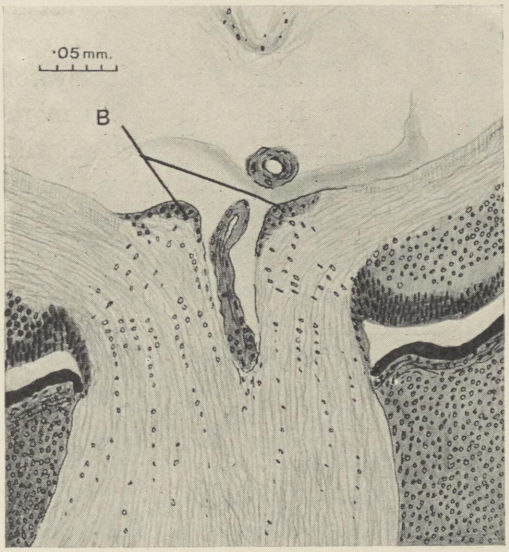


Fig. 203 *b*. Optic disc of 32 mm. human embryo. *B*, Bergmeister's papilla.

The **cilio-retinal artery** which supplies the macular region occasionally in man is developed as an enlarged anastomosis of one of the posterior ciliary arteries with a small branch of the bulb of the hyaloid artery on the disc. The *ciliary arteries* forming the circle of Zinn penetrate to a certain extent among the nerve fibres around the point of exit of the nerve. This invasion of the nerve fibres by mesoderm here is on a par with the process of vascularisation of the nerve behind the point of entry of the hyaloid mentioned above. It is apparently easy for new vessels to invade the walls of the optic cup if nerve fibres are present, but it is to be noted that no such invasion occurs in regions protected by a membrane, e.g. the membrane of Bruch or the internal limiting membrane of the retina. Anastomosis of ciliary and retinal vessels only occurs round the edge

Digitized by Illinois College of Optometry Library

of the disc in man, where traces of channels can often be found in human foetuses. In many of the lower mammals (e.g. some carnivores) these anastomotic channels enlarge and form the definitive retinal blood supply, no true arteria centralis retinae being developed. The occurrence of a cilio-retinal artery in man may perhaps have some atavistic value, although one must remember that no living animal of to-day can be looked on as having unspecialised ancestral characters.

Abnormalities

Certain abnormalities of development may arise in connection with the intra-ocular blood system. This is not surprising in view of the fact that an extremely elaborate vascular system is developed only to disappear completely before birth. As might be expected, most of the congenital abnormalities associated with this vascular system are due to its failure to disappear, in whole or in part, at the proper time. The most common portion to persist is that which is normally the last to atrophy, namely the pupillary membrane. All grades of *persistent pupillary membrane* may be met with, from complete persistence, with circulation still in progress in the vessels, down to the appearance of a minute greyish thread adherent to some part of the lesser circle. This minimal persistence is extremely common and can easily be found if a number of apparently normal eyes are examined with the slit-lamp.

Next in frequency to persistence of the *anterior portion* of the tunica vasculosa lentis is *persistence* of the *hyaloid artery*. This again may remain in whole or in part. If complete, it is usually associated with opacities and vessels on the back of the lens (one form of pseudo-glioma). If incomplete, either the lental end or the proximal end, or occasionally both (the central portion having disappeared) may persist. We have already seen that minimal persistence of the lental end is the rule rather than the exception.

Persistence of these portions of the vascular system leads to little abnormality other than the appearance of the vessels themselves, but persistence of the *lateral portion* of the tunica vasculosa lentis may give rise secondarily to other abnormalities from pressure of the vessels on growing parts. It will be remembered that the capsulo-pupillary vessels turn over the margin of the optic cup to drain into the annular vessel and in so doing may slightly indent the margin of the cup. If some of them persist they may lead to localised defects in the iris (coloboma iridis) or, if all of them persist, to one type of

Digitized by Illinois College of Optometry Library

aniridia. Defects of the iris are not necessarily associated with persistence of vessels. Other anomalies, such as adhesion of the lens to the cornea may also serve to produce them.

Occasionally an anomaly is due, not to undue persistence of mesoderm but to undue *atrophy*, as when the anterior layer of vessels of the iris stroma separates from the deeper ones, or when localised clefts and colobomata involve the stroma of the iris alone.

Opening up of normal capillary anastomoses may occasionally account for congenital vascular anomalies. This is the case in cilio-retinal arteries, optico-ciliary and choroido-vaginal veins. Small vascular channels in these situations are common in embryos but do not usually (except the cilio-retinal ones) attain sufficient size to be demonstrable clinically.

Complete absence of retinal vessels and also of the choroid have been recorded but are extremely rare. Localised absence of the vessels of the chorio-capillaris occurs in both typical and atypical colobomata of the choroid. The mode of production of an atypical coloboma of the choroid is not understood. It is generally considered to be the result of an intra-uterine inflammatory process, and to bear no relation to normal development.

B. The Ciliary Muscle

The ciliary muscle develops from *mesoderm*, and in this respect differs essentially from the sphincter and dilatator of the pupil, which, as we have seen, arise from the neural ectoderm of the optic cup. The mesoderm which gives rise to the ciliary muscle fibres is that in contact with the outer surface of the optic cup in the region of the ciliary folds (and is therefore paraxial). In this situation at 3 months can be recognised an area in which the muscle fibres themselves are just beginning to appear. This area is somewhat triangular in section, with its apex directed backwards. It is bounded internally by the neuro-epithelium of the margin of the optic cup and externally by the commencing sclerotic condensation. Its narrow base, turned forwards, abuts on the angle of the anterior chamber. Its apex is formed by the approximation of its internal and external boundaries. These relations are shewn in the diagram in Fig. 204. Within this area during the 3rd month the loose mesodermal mesh, resembling in many respects the stroma of the iris with which it is in continuity anteriorly, begins to be arranged more regularly, so that lines of cells and strands of fibres can be seen running antero-posteriorly in

Digitized by Illinois College of Optometry Library

the direction of the future meridional portion of the ciliary muscle. These fibres appear to take origin from the beginning from the position of the future scleral spur. They are in continuity with sclerotic fibres and with fibres of the uveal connective tissue of the orbiculus ciliaris, and are at first not sharply marked off from these. By the 5th month, however, the muscle can be clearly distinguished. It now forms on section a triangle within the triangle of mesoderm described above, but having its apex directed anteriorly towards its point of origin from the scleral spur. Its relations can be seen in the diagram in Fig. 205. It is bounded externally by the sclerotic, internally by the neuro-epithelium of the ciliary region and the

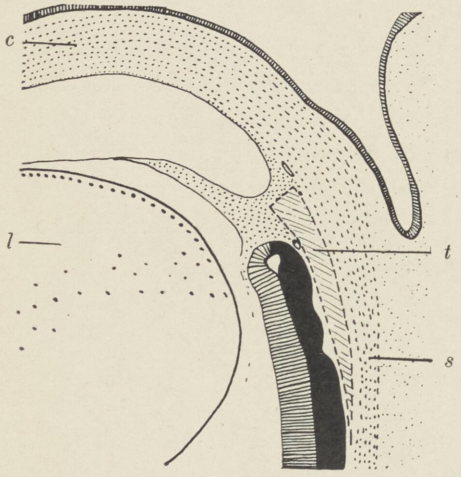


Fig. 204. Diagram shewing the triangular area within which the ciliary muscle develops. *l*, lens; *c*, cornea; *s*, sclerotic condensation; *t*, triangular area described in text.

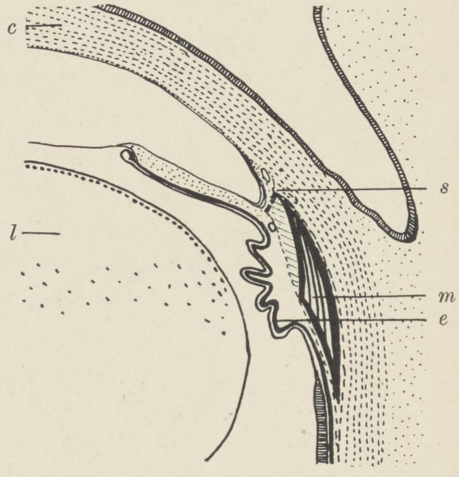


Fig. 205. Diagram shewing the relations of the developing ciliary muscle. *c*, cornea; *l*, lens; *e*, ciliary epithelium covering the processes; *m*, ciliary muscle; *s*, scleral spur.

vessels in contact with this, and antero-internally by the mesoderm at the root of the iris. There is much more of this mesoderm at 5 months than there is in the adult, so that at 5 months the point of origin of the ciliary muscle appears to be well behind the angle of the anterior chamber, and not on a level with it as it is in the adult. This alteration in the relations of the scleral spur will be dealt with more fully in describing the differentiation of the corneo-scleral junction (see p. 241). It does not affect the development of the ciliary muscle, which differentiates *in situ*. The apparent shifting forward of the muscle is due to the deepening of the angle of the anterior chamber, not to any migration of the muscle itself.

At the end of the 5th month the *meridional* portion of the ciliary muscle is well differentiated, but it is only during the 6th month

Digitized by Illinois College of Optometry Library

that the *circular* portion of the muscle can be recognised. This appears first as small muscle bundles cut transversely and lying on the inner side of the main muscle mass. They increase in size and are well formed by the end of the 7th month. The meridional portion of the muscle is complete at birth, but the circular portion continues to develop for a variable time after birth. This post-natal growth of the muscle is distinctly correlated with the amount of work it does, and is of the nature of a physiological hypertrophy. It depends primarily on the amount of hypermetropia, being large when this is over two dioptres; in other words, the size of the circular portion of the ciliary muscle is inversely proportional to the size of the whole eye.

The varying relations of the ciliary muscle to the surrounding parts can be seen in the Figs. 210, 212, 213, 214 and 215, which shew the differentiation of the angle of the anterior chamber and of the corneo-scleral junction.

C. Cornea and Sclerotic

Under the heading "Cornea and Sclerotic" must be described:

1. The differentiation of the cornea.
2. The region of the corneo-scleral junction and the differentiation of the angle of the anterior chamber.
3. The differentiation of the sclerotic in its lateral and posterior parts.

The Differentiation of the Cornea

In early stages, i.e. up to 12 mm., we have seen that protoplasmic continuity between cells of the same and of different germ layers is the rule rather than the exception. For example, we have the protoplasmic strands which unite the inner layer of the optic cup with the wall of the lens vesicle, or those which join, in early specimens, the cells of the outer layer of the optic cup with the mesoderm cells in which it is embedded. Some of these protoplasmic connections disappear before others, the signal for disappearance being the onset of histological differentiation in the cells concerned, e.g. the appearance of pigment in the outer layer of the cup or the commencement of the hyaline lens capsule. How far the ectodermal fibrillae persist among the mesoderm cells to which they are united cannot with certainty be settled, though it is possible that some of the non-nucleated fibrillar substance of the embryonic connective tissue may be ectodermal in origin.

This continuity of protoplasm holds good in early stages all over

Digitized by Illinois College of Optometry Library

the embryo, and the region of the anterior surface of the lens vesicle is not an exception. Here, before the appearance of the hyaline capsule of the lens, strands of protoplasm may be seen uniting the lens vesicle and the surface ectoderm. These strands are seen in Fig. 206, which shews the lens of a 12 mm. human embryo. There are very few mesoderm cells lying between the surface and the lens, and the fibrillar substance which separates the two has been called the "anterior vitreous," since it is formed of stretched out protoplasmic adhesions connecting two ectodermal surfaces, between which mesoderm cells are extending. This *anterior vitreous* loses its connection with the lens at 13–14 mm. and soon after can no longer be recognised. Attention has been called, however, to its possible importance in the development of the cornea by recent writers (Knape, von Szili and Seefelder). They have shewn that in birds there is evidence that its persistence is responsible for the formation of the hyaline membranes of the cornea (Bowman's and Descemet's membranes), which are thus ectodermal structures, and in part for the *substantia propria*, which can be looked on as containing both ectodermal and mesodermal elements and hence bearing a superficial resemblance to the vitreous.

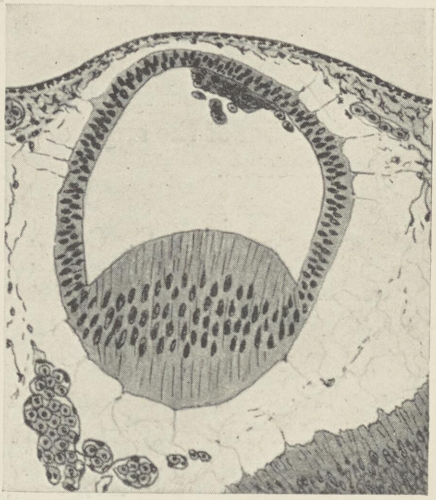


Fig. 206. Section through the lens vesicle of a human embryo of 12 mm. Note the remains of the protoplasmic adhesions stretching between the lens and surrounding structures. The surface ectoderm is seen in the upper part of the drawing and a small piece of the retinal wall on the right below.

These views, however, receive little confirmation from a study of human development. The anterior vitreous exists in man, but disappears so soon and so long before either Descemet's or Bowman's membrane can be recognised at all, that it is impossible to say whether it plays any part in the development of the cornea. It cannot be denied, however, that ectodermal fibrils are present in early stages among and joining with mesodermal processes of cells lying between lens and surface ectoderm. How far they persist and whether they increase in number and size (though this is improbable, since they are separated from their generating cells) is impossible to say.

No true cornea can be said to exist before the 18 mm. stage. There is before this merely a thin cellular lamina separating the

Digitized by Illinois College of Optometry Library

surface epithelium from the anterior face of the lens. At 18 mm., as we have seen when considering the formation of the pupillary membrane, a narrow slit appears in this mesodermal lamina, separating it into an anterior slightly thicker portion (cornea) and a posterior thin layer (pupillary membrane). This can be seen in Fig. 207 which shews the very earliest indication of a chink in the mesoderm which will eventually widen to form the *anterior chamber*. The mesoderm anterior to the narrow space can now be definitely styled the *rudimentary cornea*. It is very thin and composed of stellate mesodermal cells. There are no blood vessels in it and it is quite transparent (in common with the rest of the body of the embryo at this stage).

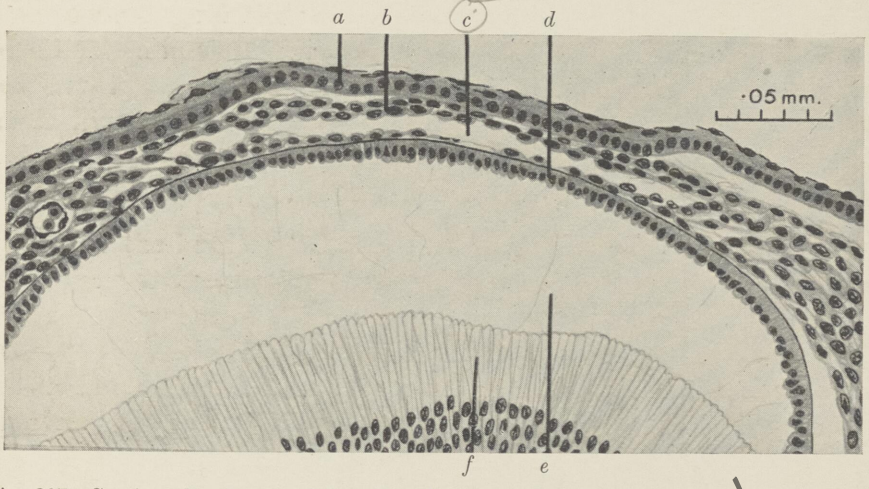


Fig. 207. Section shewing the formation of the anterior chamber in an 18 mm. human embryo. *a*, surface ectoderm; *b*, layer of mesoderm representing the future cornea; *c*, narrow interval, the first sign of the anterior chamber; *d*, the epithelium of the anterior surface of the lens vesicle covered by a single layer of mesoderm cells; *e*, cavity of lens vesicle; *f*, anterior ends of early lens fibres.

By 20 mm. this rudimentary cornea is separated by a wider interval from the pupillary membrane and a definite anterior chamber is present. The cornea itself is thicker and the stellate mesoderm cells composing it are giving rise to fibrils which by means of differential stains can be shewn to contain collagen. These fibrils are the beginning of the ground substance of the *substantia propria*. The mesoderm cells on the deep aspect of the cornea now arrange themselves in a definite limiting row and become flattened. This is the beginning of *Descemet's endothelium*; it appears towards the periphery. It is thus formed by slight rearrangement of the cells *in situ*, and does not grow from the periphery. The centre of the cornea is from the first the thinnest part.

Digitized by Illinois College of Optometry Library

Fig. 208 shews a high power view of a section of the cornea of a 25 mm. human embryo. The epithelium of the surface is two layers thick, the outer is composed of *flattened* cells, the inner of *cubical*. The substantia propria is richly cellular but avascular. Collagenous fibrils are appearing. Descemet's endothelium is composed of a single layer of somewhat flattened cells. The substantia propria shews in its deepest part a tendency to condensation. This condensation becomes more marked towards the periphery where it blends with the commencing sclerotic condensation. It increases in width as the embryo grows until finally the whole cornea appears of more solid

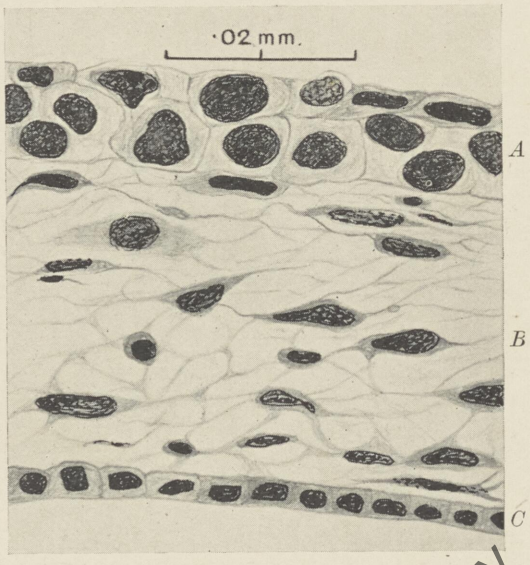


Fig. 208. High power view of a portion of the cornea of a 25 mm. human embryo. *A*, surface epithelium; *B*, substantia propria; *C*, Descemet's endothelium. Descemet's membrane has not formed yet.

and compressed tissue than formerly. While this is happening the collagenous fibrils are increasing and the nuclei relatively diminishing in number so that by 7 months the cornea resembles that of the adult in its histology.

The structureless layer (*Descemet's membrane*) lying in front of the endothelium can first be recognised with certainty at 76 mm. (Seefelder) though it probably begins to form about the 10th week (49 mm.). It appears to be homogeneous from the first, not to be formed of fibrils which subsequently coalesce. At the 4th month in the substantia propria directly in contact with it can be seen a few elastic fibres, some of them isolated, others in continuity with cells. These elastic fibres increase in length and number slightly, but are

Digitized by Illinois College of Optometry Library

always more numerous in the deeper parts of the cornea than in the superficial.

Bowman's membrane, the superficial hyaline membrane of the cornea, first makes its appearance at 103 mm. (Seefelder). Fig. 209 shews a section of the cornea at 7 months. Its similarity to the adult condition is practically complete. In early stages the *radius of curvature*

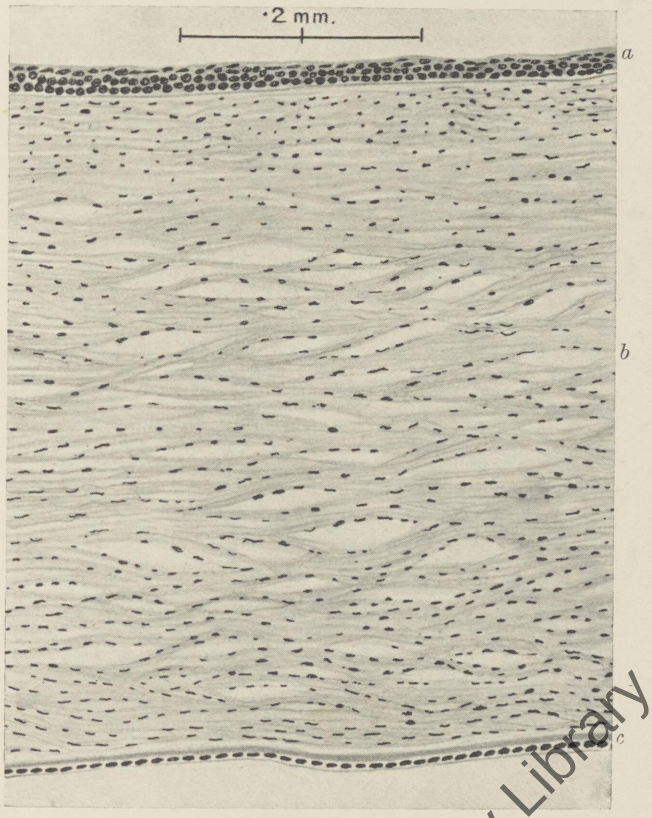


Fig. 209. Section through the cornea of a human foetus of 7 months. *a*, surface epithelium; *b*, substantia propria; *c*, Descemet's membrane and endothelium.

of the cornea and of the sclerotic is the same; the increased curve of the cornea is not apparent until the 4th month, when the *corneo-scleral junction* can be easily recognised and the two curvatures distinguished.

2. The Region of the Corneo-scleral Junction and the Differentiation of the Angle of the Anterior Chamber

When the anterior chamber first appears its diameter is not relatively so great as it is finally. The angle is blocked by mesodermal tissue continuous with the pupillary membrane, and this mesodermal

Digitized by Illinois College of Optometry Library

tissue shares in the process of atrophy which involves so much of the embryonic mesoderm associated with the optic cup. The consideration of the differentiation of the associated mesoderm at the corneo-

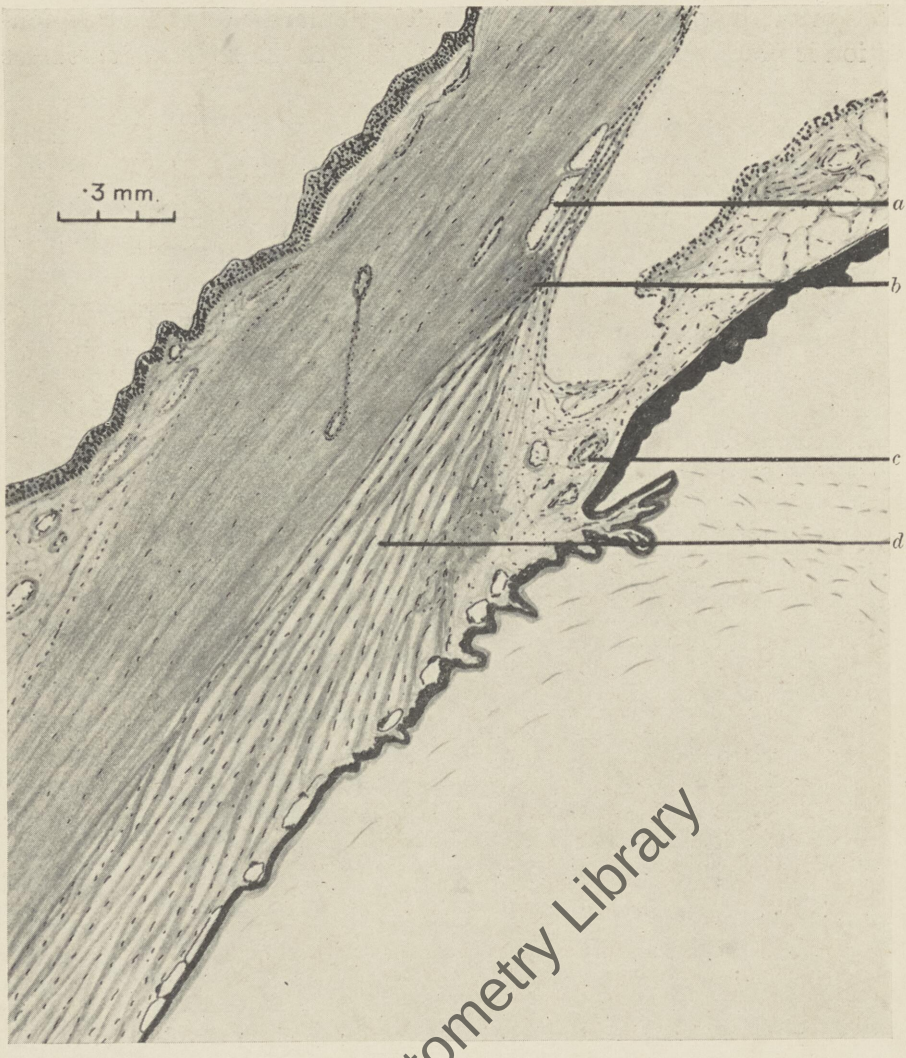


Fig. 210. Section through the angle of the anterior chamber in an adult human eye. *a*, canal of Schlemm; *b*, scleral spur; *c*, circulus arteriosus iridis major; *d*, ciliary muscle.

scleral junction involves a study of the altering relations of the angle of the anterior chamber to the neighbouring vessels (circulus arteriosus iridis major and circulus venosus Schlemmii (canal of Schlemm)) and to the origin of the ciliary muscle.

These alterations can be best realised by studying in detail five successive typical stages and comparing them with the adult condition.

Digitized by Illinois College of Optometry Library

Fig. 210 shews the region of the angle in an adult human eye. The main points of note are:

1. The *canal of Schlemm* lies anterior to the scleral spur, well in front of the bottom of the angle of the anterior chamber.

2. The *origin of the ciliary muscle* from the scleral spur is just in front of the bottom of the angle.

3. The *circulus arteriosus iridis major* lies on a level with or slightly behind the deepest part of the angle.

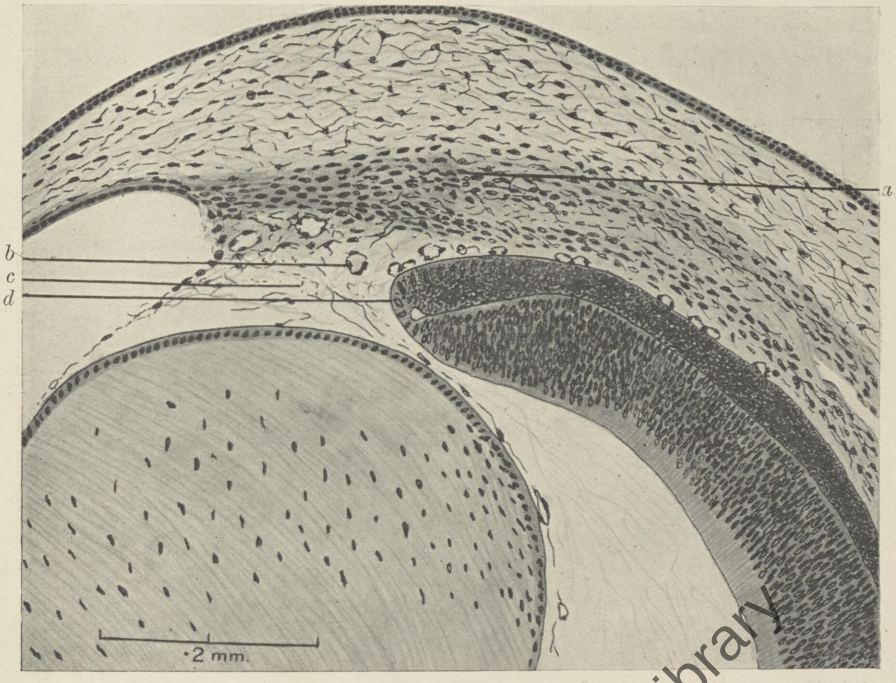


Fig. 211. Section through the angle of the anterior chamber in a 25 mm. human embryo. *a*, band of sclerotic condensation; *b*, circulus arteriosus iridis major; *c*, mesoderm continuous with pupillary membrane; *d*, margin of optic cup.

These three structures, canal of Schlemm, origin of ciliary muscle, and major circle therefore lie, roughly, one behind the other in this region. Throughout development they occupy the same positions relatively to each other, while the position of the angle of the anterior chamber relatively to them shifts continually backwards, and the margin of the optic cup continually forwards, during embryonic life. They may therefore be taken as fixed points in estimating the rates of growth and atrophy of other structures in this region. Fig. 211 shews the region of the angle in a 25 mm. human embryo. The margin of the optic cup reaches only to the equator of the lens and in front of this lies a mass of mesoderm in which there are already

Digitized by Illinois College of Optometry Library

signs of active differentiation. The cornea shews a definite band of condensation in its deepest part, and this runs backwards from the angle around the outside of the cup in the line of what will eventually be the deepest part of the sclerotic. *Outside* this line of condensation can be seen, in the corneal region, the imperfectly differentiated substantia propria, and in the region of the corneo-scleral junction and behind this, a richly cellular undifferentiated embryonic connective tissue, which will eventually form the more superficial layers of the sclera, the episclera and the conjunctiva. *Inside* this line of condensation can be seen, in the most anterior part, the endothelium of the cornea, behind this a mass of loose meshed mesoderm continuous

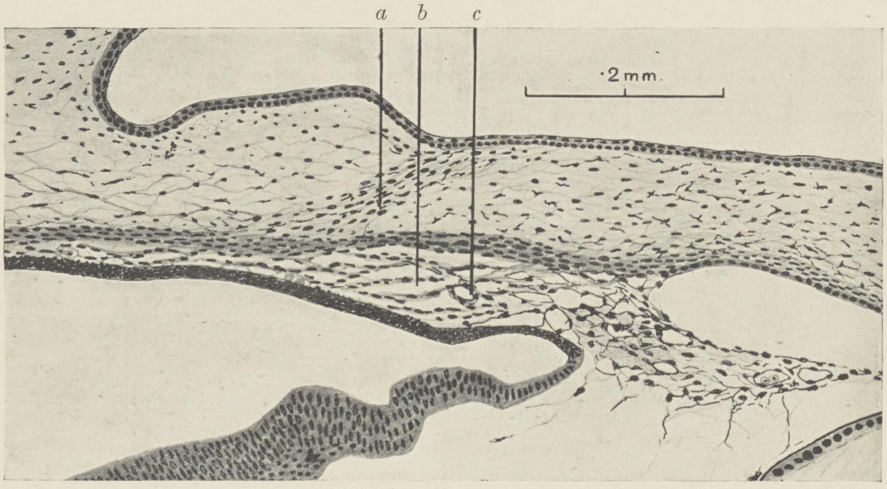


Fig. 212. Section through the angle of the anterior chamber in a 48 mm. human embryo. *a*, condensation in overlapping portion of sclera; *b*, ciliary muscle *anlage*; *c*, circulus arteriosus iridis major.

with the pupillary membrane and bounding the angle of the anterior chamber, and behind this, again, a more richly cellular mesoderm forming a faintly marked band stretching backwards from behind the angle towards the choroid, with which it blends. The major circle of the iris can be seen lying deep to this band, just in front of the margin of the cup and well behind the angle of the anterior chamber. At this stage the canal of Schlemm cannot be found, and the scleral spur is not developed. The cellular band of mesoderm inside the scleral condensation represents, however, the *anlage* of the ciliary muscle, and it will be seen that it blends with the scleral condensation just in front of the major circle, and well behind the angle of the anterior chamber. The angle therefore is markedly anterior to its definitive position.

Fig. 213 shews the same region at 48 mm. when growth of the

Digitized by Illinois College of Optometry Library

ectodermal iris is just about to commence. The corneo-scleral condensation is much more marked. It involves the posterior layers of the cornea and runs backwards as a thick band towards the equator of the eye. On its *outer* side the uncondensed part of the substantia propria can be seen as before, blending laterally with the conjunctival and episcleral tissues, but here a slight differentiation has occurred since the last stage, namely the appearance of a faint area of condensation marking the position of the most anterior portion of the

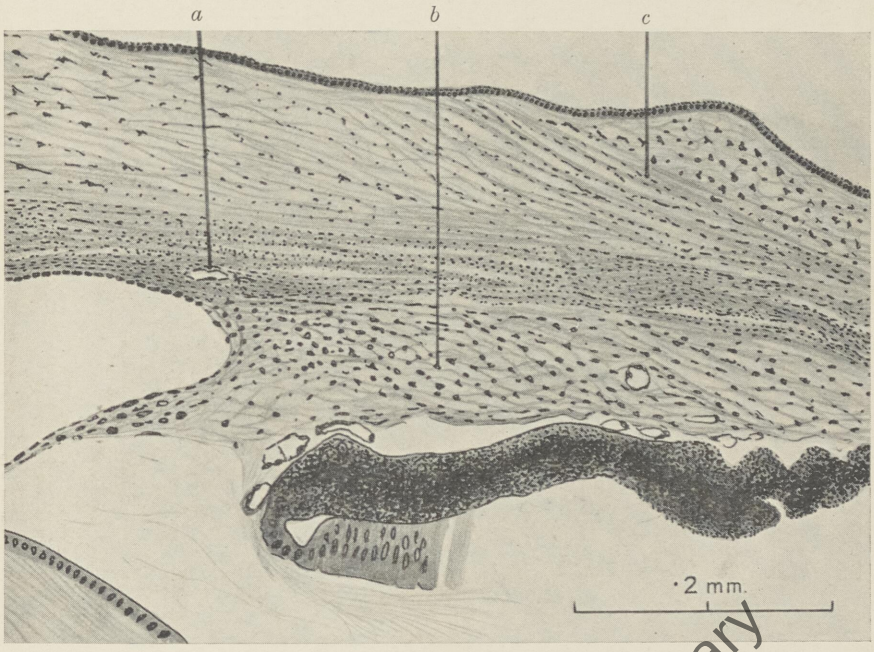


Fig. 213. Section through the angle of the anterior chamber of a 65 mm. human embryo. *a*, canal of Schlemm with condensation marking the scleral spur just to the right of it; *b*, ciliary muscle rudiment; *c*, corneo-scleral junction.

sclera where it overlaps the corneal margin. This is the first sign of condensation in the outer layers of the sclera.

On the *inner* side of the line of deep scleral condensation can be seen, as before, a region of loose mesoderm associated with the root of the iris and the ciliary region. The distance from the margin of the optic cup to the angle of the anterior chamber is here less than it was at the previous stage, since the ectodermal iris has just started to grow. The relations of the angle to the major circle and to the ciliary muscle *anlage* remain, however, unchanged. The position of the scleral spur is faintly indicated and the lines of condensation in the muscle rudiment shew the future direction of its fibres, but no true muscular tissue is present until the next stage. This is seen in

Digitized by Illinois College of Optometry Library

Fig. 213 which shews the same region in a 65 mm. embryo. The line of deep corneo-sclerotic condensation is not so marked, since the condensation is now much more general and the superficial layers of the *sclera* can be distinguished from the *episclera*. The sclera still appears a good deal thinner than the cornea. The inner edge of the corneo-sclera is well marked, and a small venous channel, the *canal of Schlemm*, can be seen among the fibres of it. This lies on a level

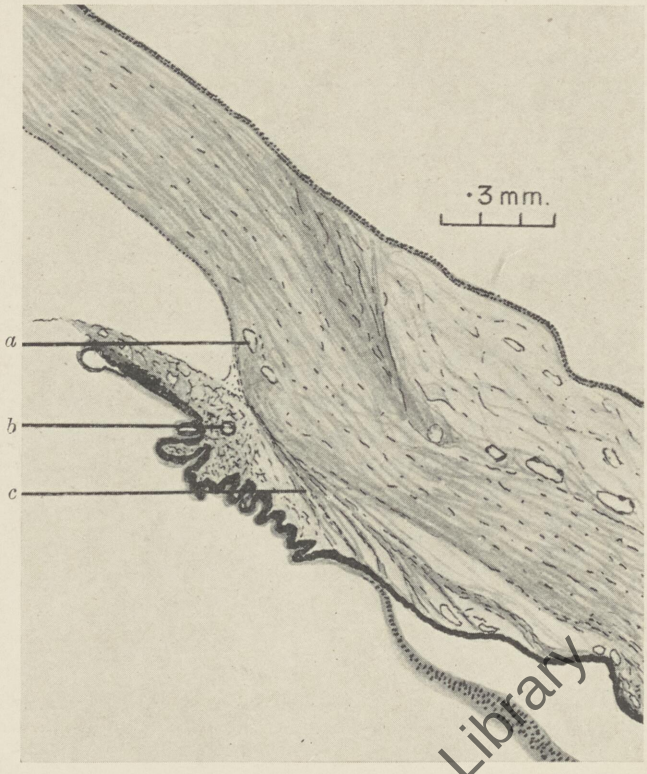


Fig. 214. Section through the angle of the anterior chamber of a 5 months human foetus. *a*, canal of Schlemm; *b*, circulus arteriosus iridis major; *c*, ciliary muscle.

with the deepest part of the angle, and not in front of this, as it does in the adult[1]. Behind it the position of the scleral spur and the *anlage* of the ciliary muscle can be seen, the latter now more definitely muscular. Deep to this, the tip of the ectodermal iris can be seen to have grown forward till it lies on a level with the angle, not right behind it, as it does in Figs. 211 and 212. The bottom of the angle also lies nearer the major circle than in previous stages, showing that

[1] The canal of Schlemm at this stage is deeply embedded in mesoderm. The open mesh of the spaces of Fontana is formed by atrophy of this mesoderm between the canal and the angle of the anterior chamber. This atrophy is probably only completed during the eighth month.

Digitized by Illinois College of Optometry Library

there has been both a forward growth of the ectodermal iris and a deepening of the angle. These processes continue, the forward growth of the ectoderm far exceeding in rate the atrophy of the mesoderm at the bottom of the angle. This mesoderm at this stage appears densely cellular and sharply limited towards the angle. In subsequent stages it becomes more open in texture, and spaces appear in it. Its atrophy coincides with and appears to be a similar process to the atrophy of the lateral and anterior portions of the tunica vasculosa lentis.

By 5 months (Fig. 214) the canal of Schlemm lies well in front

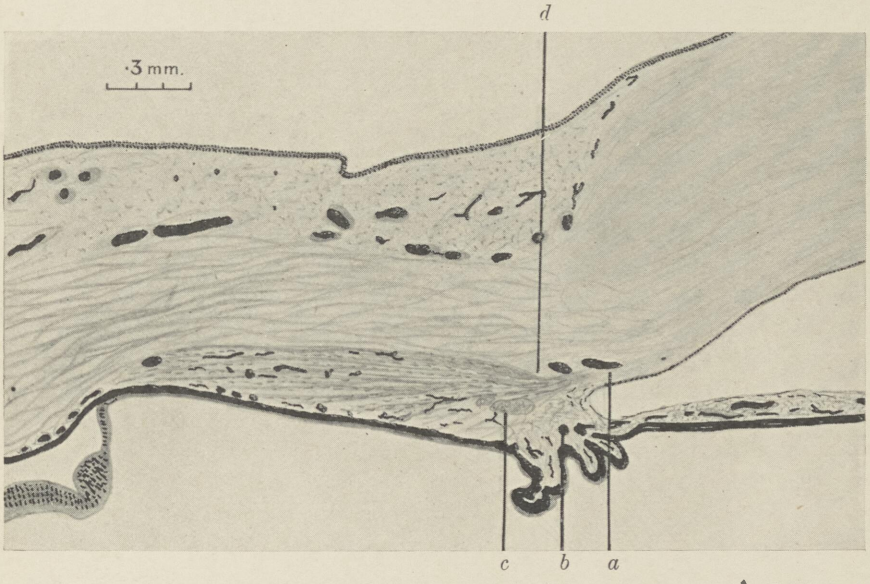


Fig. 215. Section through the angle of the anterior chamber of a human foetus of 7 months. The vessels have been injected with Indian ink. *a*, canal of Schlemm; *b*, circulus arteriosus iridis major; *c*, circular fibres of the ciliary muscle; *d*, scleral spur.

of the bottom of the angle and the ectodermal iris is far advanced. The meridional fibres of the ciliary muscle are strongly developed and take origin from the scleral spur. The circular fibres have not yet appeared. The corneo-scleral junction is quite obvious and the increased *corneal curve*, which is not apparent in the earlier specimens, well developed.

By 7 months (Fig. 215) the condition more nearly resembles that in the adult. The angle has opened up still further, but not completely, for the canal of Schlemm is not entirely in front of it yet. The scleral spur is easily seen, but lies still well behind the bottom of the angle. The *circular fibres* of the *ciliary muscle* have appeared. The scleral condensation is thicker and more markedly different from the loose subjunctival tissue. The iris is well grown. The major circle lies behind the angle. The tissue in the angle is loose and open.

Digitized by Illinois College of Optometry Library

Atrophy of this progresses still further, with the result that finally (just before birth) the adult condition is reached and the canal of Schlemm and the scleral spur both come to lie in front of the bottom

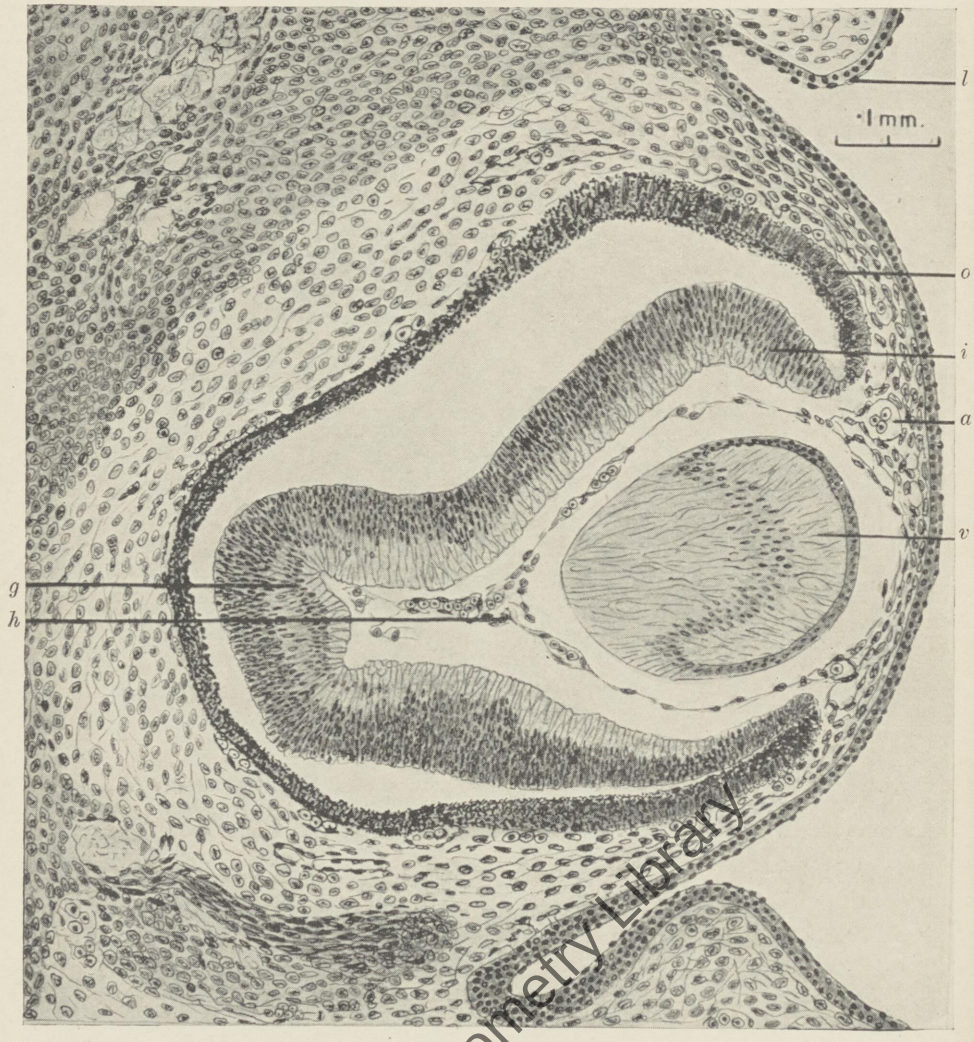


Fig. 216. Section through the eye of a 15 mm. human embryo. The annular vessel is seen in section at *a*. The lens (*v*) is surrounded by its vascular capsule formed by the branching of the hyaloid artery at *h*. Other points of interest in this section which should be noted are: *l*, the commencing lid-fold covered with surface ectoderm which shews very clearly the divisions into epitrichial and nervous layers; *g*, the area of commencing differentiation of the inner layer (*i*) of the optic cup at the posterior pole; also the wide separation between the outer layer (*o*) and the inner layer of the cup and the absence of an anterior chamber.

of the angle (Fig. 210), while the major circle lies on a level with it. Thus the vein, the spur and the artery have not changed their relative positions to each other but merely to the angle and the ectodermal iris.

Digitized by Illinois College of Optometry Library

3. The Differentiation of the Sclerotic in its Lateral and Posterior Parts

The *sclera* differentiates by condensation from the mesoderm encircling the optic cup. In the earliest stages, up to 18 mm., there is

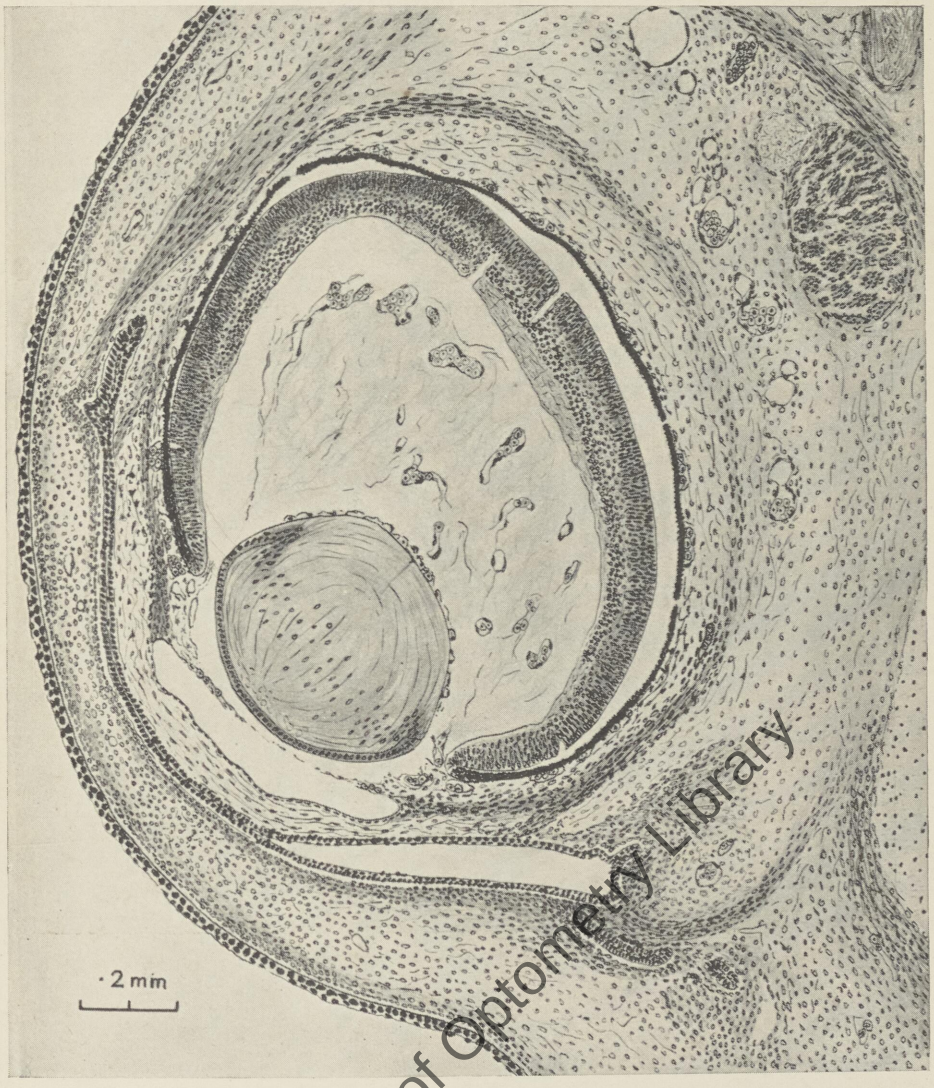


Fig. 217. Section through the eye and surrounding structures in a 35 mm. human embryo.

no distinction of layers in the mesoderm in which the cup is embedded (Fig. 216 shews the 16 mm. stage). Soon after, the cells of the mesoderm nearest the cup tend to become arranged with their long axes parallel to its wall, and almost immediately (19–20 mm.) some

Digitized by Illinois College of Optometry Library

indication of a condensation appears, running from the region of future attachment of the extrinsic muscles forward to the angle of the anterior chamber, where it becomes continuous with a condensation in the posterior layers of the sclera in its anterior part. Behind the equator there is no trace of a line of demarcation between

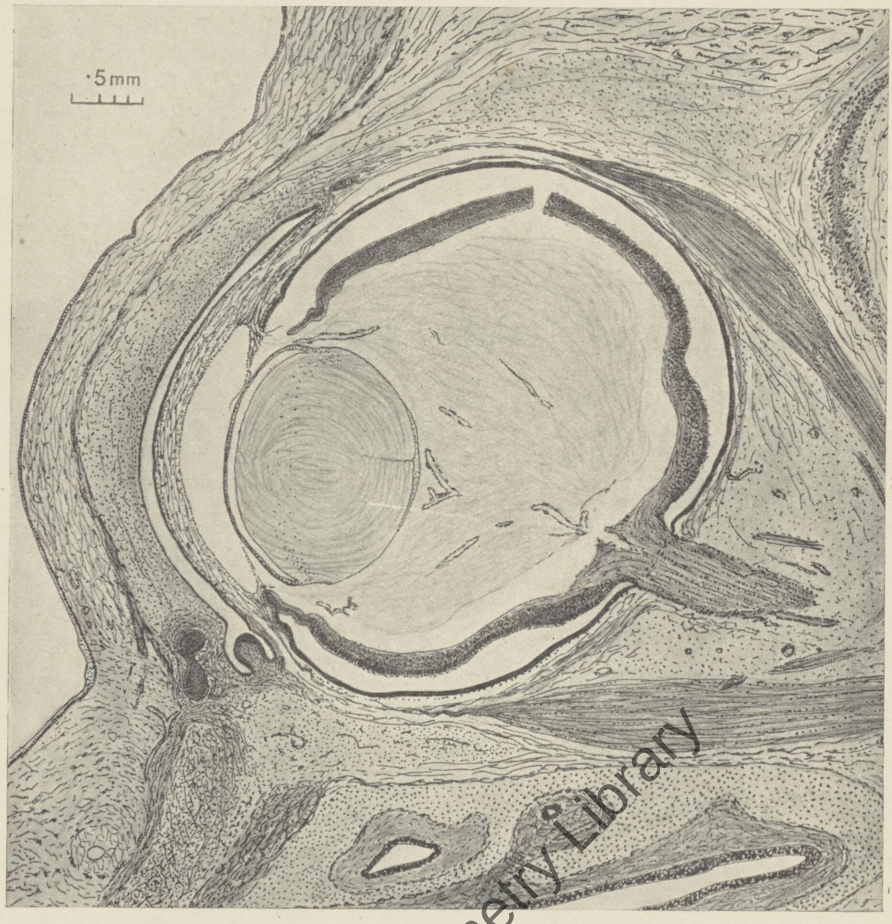


Fig. 218. Section through the eye and orbit of a 3 months foetus.

choroid, sclera, or orbital tissue at all. The extrinsic muscles can be recognised at this stage forming a sort of funnel around the eye, and the sclerotic rudiment blends with this and fades away along it. By 35 mm. a very faint condensation, some little distance away from the eye, can be seen at the posterior pole (Fig. 217), and by 65 mm. this has increased and approached nearer to the choroid (Fig. 218). Thereafter, (4th month) development of the posterior parts proceeds apace, and by *five months* the sclera is well differentiated all the way round.

Digitized by Illinois College of Optometry Library

This lagging behind in development of the posterior part of the sclera is of interest when it is realised that, in some of the lower animals, where differentiation of the sclera progresses further to the formation of cartilage or bone (Amphibia and Sauropsida), the anterior portions of the sclera are those which shew the most advanced stages, while posteriorly, around and especially below the entrance of the nerve, the sclera often remains in the more primitive fibrous stage. It appears to be a general rule that the anterior portion of the sclera should appear first and progress farthest during embryonic life in all species. This may also be correlated with the fact that in the pathological

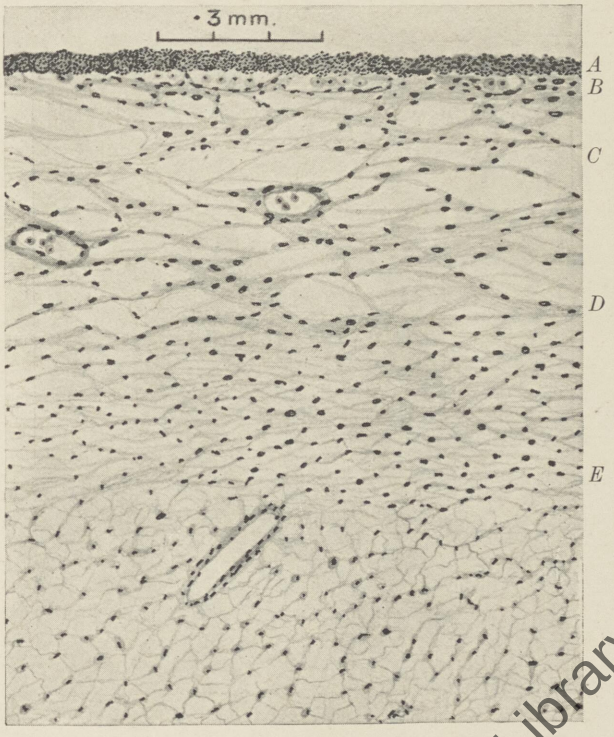


Fig. 219. Section through the choroid and sclerotic of a 65 mm. human embryo. *A*, pigment epithelium of retina; *B*, chorio-capillaris; *C*, layer of larger vessels (venous); *D*, inner surface of sclerotic condensation; *E*, outer surface of sclerotic condensation.

condition of progressive myopia (of the developmental origin of which there is considerable evidence) it is the posterior part of the sclera which suffers the greatest stretching and deformity.

Figs. 219 and 220 shew the sclera at the posterior pole at two typical stages, namely soon after its commencement at 65 mm. and at 5 months. The collagen fibrils probably develop within the protoplasm of the cells themselves. They appear earlier in the anterior than the posterior part. During the 5th month *chromatophores* begin to be recognisable on the inner surface of the sclera, in the lamina supra-choroidea.

Digitized by Illinois College of Optometry Library

Abnormalities

Certain anomalies may arise in the course of development of the cornea and the sclerotic. In the *first* place, the alteration in the corneal curve noticed at the 5th month may not occur, and the cornea and sclerotic may thus come to have the same radius of curvature, a condition of *flat cornea* usually associated with microphthalmos. *Secondly*, the atrophy of the mesoderm of the angle of

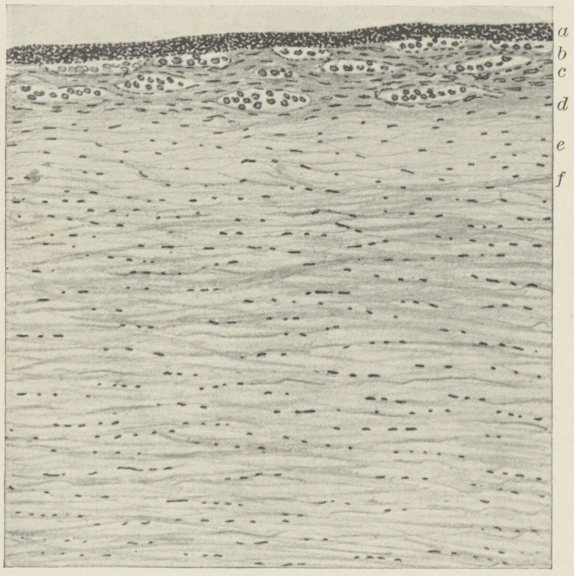


Fig. 220. Section through the choroid and sclerotic at 5 months. *a*, pigment epithelium of retina; *b*, chorio-capillaris; *c*, intermediate layer of vessels (arterial); *d*, outer layer of vessels (venous); *e*, lamina supra-choroidea; *f*, inner surface of sclerotic.

the anterior chamber may fail to occur, with the result that the filtration angle is blocked, and, when the ciliary glands begin to secrete aqueous humor, the tension rises and a condition of *buphthalmia* or congenital glaucoma results. Again, as mentioned above, the posterior portion of the sclera may remain permanently thinner and weaker than the anterior, and may therefore give way under the normal intra-ocular tension, producing a *posterior staphyloma*. These three abnormalities may be looked on as results of simple arrests of development.

Digitized by Illinois College of Optometry Library

VII

THE ORBIT AND ITS CONTENTS

A. The Extrinsic Ocular Muscles

The *extrinsic ocular muscles* in man are developed essentially as condensations in the *paraxial mesoderm* surrounding the optic vesicle. The initial stages of development of the mesoderm of the head in human embryos are definitely abbreviated, so that it is not possible without resort to comparative observations to establish any conclusive facts with regard to the presence of metamerism in the head region in man and to the relation between the paraxial musculature and the various head segments.

In order to get any idea of the phylogeny of the ocular muscles one must study the development of a vertebrate sufficiently simple to shew the origin of the mesoderm of the head. This can be studied in the embryo of the dogfish, *Acanthias*. In this animal, the head shews the presence of definite cavities, which are evidently in series with those of the somites (or myotomes) behind them, and can therefore be looked on as somitic (or myotomic) in value. There are four of these cavities on each side but these probably do not represent the total number of myomeres (myotomes) which have been taken up into the head during evolution. They at least constitute a much more primitive arrangement than that found in man and so will be of some assistance in gaining a morphological conception of the subject.

The *head cavities* of the dogfish are usually numbered from before backwards as *A*, 1, 2 and 3, *A* having been discovered subsequently to the naming of the other three. The most anterior cavity, *A*, is small, oval in form and lies just above the eye. The second, or No. 1, as it is usually termed, has a rather irregular outline and lies close behind *A*, level with the extreme anterior tip of the notochord. It is often called the *premandibular head cavity*. The next (No. 2), is the *mandibular head cavity*. It is much the largest of the four. It lies completely behind the eye and has a narrow prolongation which passes backwards and downwards towards the pharyngeal region. The last (No. 3), is a small rounded cavity lying alongside the notochord immediately behind the main portion of the mandibular cavity. The relations of these four cavities to each other and to the notochord and its adjacent myotomes are shewn in Fig. 221.

Digitized by Illinois College of Optometry Library

From the walls of the head cavities are formed certain of the paraxial muscles of the head, in the same way as the paraxial somatic muscles are formed from the walls of the myotomes lying beside the notochord further back.

From the walls of the first, or *A* cavity, is formed a mass of cells which become lost in the surrounding mesoderm.

From the walls of the premandibular cavity muscle cells are formed which grow towards the eye and gain attachment to it. There are four main outgrowths from this cavity corresponding to the rudiments of the *superior*, *inferior* and *internal recti* and the *inferior oblique*, namely, those muscles which are supplied by the oculo-motorius, the nerve of supply to this head segment. The exact portions of the wall of this head cavity which give rise to the various muscles vary in different species. There is never any variation in the muscles themselves, those supplied by the 3rd nerve always arising from the premandibular myotome.

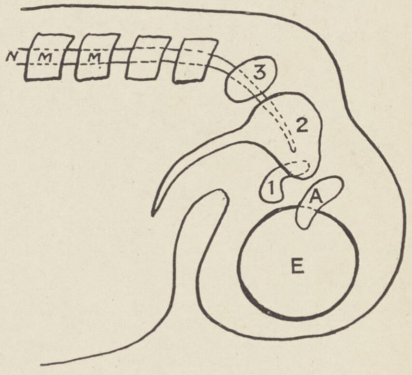


Fig. 221. Scheme shewing head cavities in the dogfish *Acanthias* (after Platt) *A*, 1, 2, 3, the head cavities; *E*, the eye; *N*, the notochord; *M*, somatic myotomes.

From the walls of the mandibular cavity comes the rudiment of a single eye muscle, the *superior oblique*, the nerve to this, the next head segment, being the trochlearis, while the last head cavity gives rise to the *external rectus muscle* and has the abducens as its segmental nerve.

A consideration of this arrangement helps us to understand the underlying meaning of the human extrinsic ocular muscles, but it must be remembered that in man the presence of head cavities is not known to occur. Moreover, the eye muscles in man seem, at their earliest stage, to be represented by a single undifferentiated mass. The earliest trace of these muscles in man can be seen at 7 mm. when they are represented by a massed condensation in the paraxial mesoderm surrounding the optic vesicle. There is at first no separation between individual muscle condensations. The distinction occurs fairly quickly. The four *recti* and the two *obliques* can be recognised as distinct before the 20 mm. stage. The separation is first apparent at their insertions and gradually spreads proximally towards their origins. At 20 mm. the *levator palpebrae superioris* is not yet to be found. It arises, soon after this stage, by a separation of some of the fibres of the medial border of the *superior rectus*, so that at first it

Digitized by Illinois College of Optometry Library

can be found lying to the inner side of that muscle and not above it (Henkel). This is the case at the 60 mm. stage. It increases in size, however, once it has separated from the superior rectus, and starts to grow laterally on a slightly higher plane, so that, at the 75 mm. stage, it overlaps the inner edge of the superior rectus. This lateral growth continues until the 4th month, when the muscle has reached its final position. As pointed out on p. 44, this alteration of the relations of the superior rectus and the levator palpebrae superioris has been adduced as evidence that the globe rotates on its long axis during development. It is, however, now admitted that the alteration of position is brought about solely by growth of the muscle and not by movement of the globe itself. The comparatively late appearance of the levator is of clinical interest when it is realised that it may entirely fail to separate from the superior rectus (which in these cases may itself be defective), thus leading to a condition of congenital ptosis with or without defective power of upward movement of the globe.

The *orbicularis palpebrarum* is part of the platysma or facial musculature which is derived from the *second visceral arch*. Cells from this arch begin to grow out (about the stage of 10–12 mm.) both backwards and upwards. These latter cells, spreading over the mandibular arch in front of them, reach the face, lying just under the dermis, and surround the eye at about the stage of 16 mm. The sheet of the orbicularis is represented in this way at this stage: minor modifications occur in it subsequently and in its later stages it extends slowly into the lids. *Riolan's muscle* cannot be recognised as separate from the orbicularis mass until 62 mm. by which time the lid margins are adherent and the rudiments of the cilia apparent.

The capsule of Tenon. The capsule of Tenon, like the sclerotic, is first recognisable in its anterior part. The rudiment of that portion of it which is related to the insertions of the recti muscles is recognisable at 80 mm. as a thin sheet of differentiating connective tissue. The posterior part is not recognisable in its full extent until the middle of the 5th month.

B. The Lids and Lacrimal Apparatus

In order to gain a clear idea of the formation of the lids and the lacrimo-nasal passages one must consider the growth of the maxillary process and the associated structures as seen from the surface. The following account is based on the work of Prof. J. E. Frazer, to whom Figs. 222, 223, 224 and 225 are also due.

Digitized by Illinois College of Optometry Library

At the beginning of the 2nd month the maxillary process, lying below the eye on each side, extends forwards as far as the opening of the nasal pit, coming into contact with the two folds (*inner and outer nasal folds*) which make the boundaries of its opening. The maxillary process thus lies in contact, along the whole of its upper border, with the paraxial mesoderm encircling the eye and primitive nose. The scheme in Fig. 222 shews this. It represents the condition of the left side of the face of an embryo of about the 12 mm. stage. The eye (*Op*) is embedded in paraxial mesoderm which is continuous in part with that making the outer nasal fold (*N*). Below this level

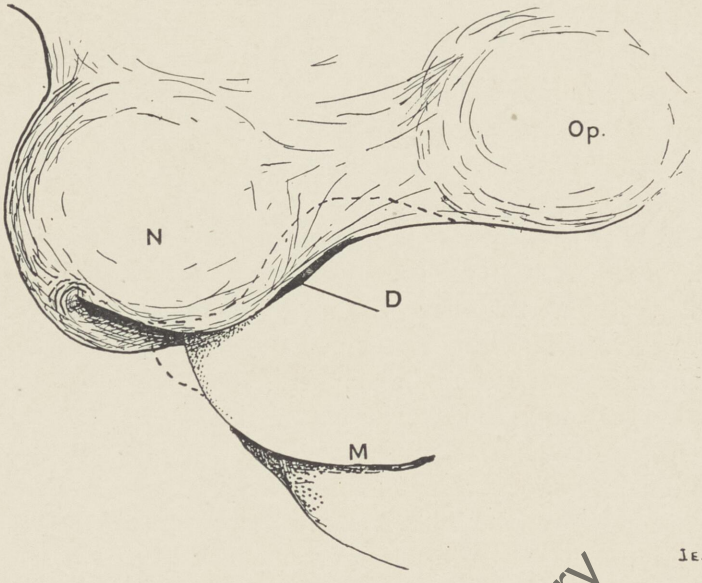


Fig. 222. Schematic reconstruction of the maxillary and nasal region of a human embryo of 11–12 mm., seen from the side. *Op.*, optic vesicle; *N*, outer nasal fold; *D*, thickened ectoderm in groove between visceral and paraxial mesoderm; *M*, the mouth.

is the maxillary process, reaching the lower and back part of the outer nasal fold. *M* is the mouth, and the mandibular arch is indicated below *M*. It can be understood from this diagram that a groove on the surface marks the line of apposition of maxillary and paraxial portions. The ectoderm in the groove between them is especially thickened at *D*. This is the first indication of the nasal duct, or, at any rate, of the duct system. The groove in which this rudiment lies can be followed down, to turn round below the outer nasal fold and so reach the nasal pit. Above, it reaches the area below and in front of the eye.

The maxillary process now begins to extend rapidly. The interrupted line in Fig. 222 gives an idea of the direction of this extension,

Digitized by Illinois College of Optometry Library

forwards and upwards. It grows along the lower aspect of the outer nasal fold, which it also overlaps laterally, while its upper part folds itself somewhat over the paraxial region between the eye and *D*. It is necessary to understand the nature of this overgrowth, which is essentially at first an overlapping of the paraxial region concerned, the extension shewn by the interrupted line, for example, turning over the line of the groove as a sort of hinge line, and applying itself to the area beyond this. Thus the upper part of the overgrowth is now separated from the paraxial structures by an ectodermal field continuous round the margin of the overgrowth with the ectoderm covering the region of the eye: below this the ectoderm between the overlapping growth and the lateral aspect of the nasal region quickly disappears, leaving the original thickening *D* now buried under maxillary mesoderm. It is thus evident that the ectoderm *D* is continuous above with the new field of ectoderm lying deep to the upper overgrowth and in this way a connection is already produced with the ectodermal lining round the eye.

The lower part of the orbital groove is also covered in by the growth, but here the margin of the outer nasal fold remains free and forms the front part of the lower turbinal mass, whence it comes about that the groove—i.e. the line of the nasal duct—leads finally to the meatus below this bone.

We have now accounted for the general line and position of the duct and also for its continuity with the ectoderm below and in front of the eye, that is, with the lower lid, but the upper canal has still to be formed before the structures can be moulded into their final shape.

At a slightly later stage, about 16 mm. the conditions are as shewn diagrammatically in Fig. 223. The rapid growth of the maxillary process has led to its projection below the eye, so that there is now a definite shelf-like lower lid. This fades in part into the upper part of the overgrowth, deep to which is the ectodermal field already mentioned, continuous below with the original thickening *D*. In the figure these buried parts are shewn as a dotted area, which is continued to the surface above the overgrowth. The continuity with the nasal cavity below is not indicated: for certain reasons it seems probable that the ectodermal line is really continuous, but about this time it appears to be broken, a fact possibly only pointing to temporary cessation of activity associated with the rapid mesodermal growth changes taking place in this part. The connection becomes re-established, and again becomes evident, at a much later stage and need not be referred to again.

Digitized by Illinois College of Optometry Library

There is as yet no indication of the mode of formation of the upper canaliculus, but a change is already apparent above the eye. In Fig. 222 there is no appearance of a lid, and the mesoderm covering the brain makes, at this stage, the only representative of a fold above the eye. In Fig. 223, however, a new element is appearing (*C*) between the brain fold and the eye. This new fold is apparently produced by extension of part of the orbital mesoderm[1] and, growing outwards, produces a definite sharp edge, a true lid, beginning to overlap the eye. This outgrowth, and consequently the lid, comes to an abrupt end further forward and now the brain fold again lies immediately above the sensory paraxial layer. As the brain has grown considerably it is sharply marked off from the nasal processes, and the deep groove between them is thus continuous with the groove between the "brain fold" and the sensory paraxial region.



Fig. 223. Schematic reconstruction of the maxillary and nasal region of a 16 mm. human embryo, seen from the side. *C*, upper lid fold; *D*, ectodermal thickening (buried).

A little later than this, about the 18 mm. stage, the upper lid has extended forwards and backwards, meeting the lower (maxillary) lid behind to form the *outer canthus* (Fig. 224). In front there is an extension downwards, between the eye and the groove separating nose and brain. This extension may be simply from the earlier one (*C* in Fig. 223), but is, more probably, a distinct formation growing in a similar way from orbital mesoderm and only secondarily continuous with the first growth. However it may be originated, the new formation grows downwards and forwards and shews two main parts: one of these (*A* in Fig. 224) extends on to the groove between nose and brain and blocks the continuity between them and the region round the eye, while the other (*B*) grows down in front of the projecting eye, overlapping the underlying structures and meeting the upper end of the maxillary growth in this situation. Thus the growth *B* covers in an ectodermal plate, which is necessarily continuous with

[1] Associated with the upper musculature.

Digitized by Illinois College of Optometry Library

that under cover of the maxillary upgrowth and hence with the original duct system. Putting it shortly, it may be said that a part of the ectodermal surface in front of the eye is covered in to form the canalicular field, the upper part being covered in by a downgrowing overlap from the upper lid, and the lower part by an upgrowing overlap from the lower lid. The buried field thus produced is necessarily (from its mode of formation) continuous with the ectoderm of the buried groove.

In Fig. 224 the buried area is indicated by the dotted line (*D*), but it should be understood that a large part of the hidden ectodermal field is broken up as the covering "flaps" meet the underlying surfaces, leaving only the cell tracts which mark the upper and lower

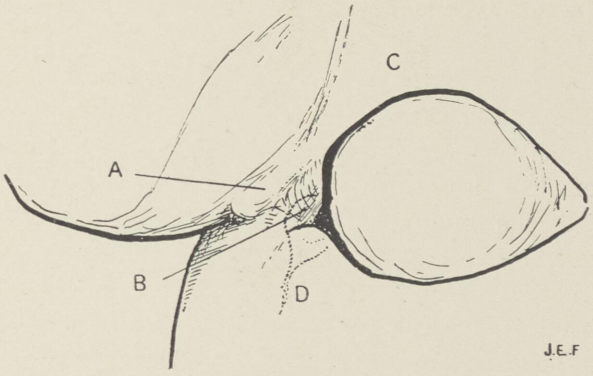


Fig. 224. Schematic reconstruction of the region of the eye and inner canthus in an 18 mm. human embryo. *A*, extension of mesoderm between eye and "brain fold"; *B*, downward prolongation from this; *C*, upper lid fold; *D*, lachrymal passages.

and deeper parts of the field. These persistent parts are the rudiments of the upper and lower canaliculi. In this way the two canaliculi come into being, each continuous with the ectoderm near the margin of its own lid.

There now ensues a period of growth and elongation of the lids, as a result of which they gradually cover the projecting eye and meet over it. The growth is apparently more effective towards the inner end, so that the lids begin to close, from within outwards, at about the 32 mm. stage. Their margins meet and ectodermal fusion (or, more accurately, adhesion) takes place between them. It is complete at 37 mm. and persists till shortly before birth. Hence the formation of glands, etc. in the lids takes place while they are fused (p. 263) and it is only after these formations are completed that cornification of the superficial cells in each lid leads to separation.

The line of the fused lids, about the time of their complete closure,

Digitized by Illinois College of Optometry Library

is shewn in Fig. 225. The greater activity at the inner end has probably been accompanied here by a certain amount of sinking of the level of the conjunctival floor. At any rate, the canaliculi, opening at first close to or at this floor, are now opening on the raised parts of the lids. There has also been a little lengthening of the lower lid relatively to the upper one in this region, for the lower canaliculus opens further out than the upper, both on very definite eminences. This relationship of the openings to each other persists in the adult, but the eminences become relatively much smaller. The lumen of the canalicular system is at first completely blocked by epithelial cells. These begin to soften at about the 50 mm. stage so that true canalisation starts soon after this. In some instances it is not complete at birth, and hence a condition of congenital lacrimal obstruction is produced. This is simply due to a delay in canalisation and is not in its origin inflammatory.



J.E.F

Fig. 225. Schematic representation of the line of the fused lids of a human embryo during the 3rd month. The dotted lines shew the position of the upper and lower canaliculi.

The region between the eminence of the lower punctum and the inner fornix is covered by a mass of thickened ectoderm, represented as a dotted area in Fig. 225. This part of the lid margin develops into the *caruncle*, its deeper aspect facing somewhat outwards and secondary margins forming round it to mark off the *lacus lacrimalis*. The actual separation of the caruncle from the lid margin occurs at 58 mm.

While these changes are going on, the *plica semilunaris* is developing. About the time that the inner ends of the lids are coming together (32 mm.) the plica is first apparent as a fold, forming a crescentic line, projecting from the conjunctiva along the inner aspect of the eye. Growth goes on fairly rapidly, so that, before long, the plica semilunaris is a well-developed membraneous fold applied to the inner aspect of the eyeball, and extending a very little more below the level of the palpebral fissure than above it. The formation of the fold seems to be due to overgrowth of orbital mesoderm, as in the case of the upper lid, but the overgrowth is much less well-marked and its existence less certain. At 55 mm. ectodermal thickenings can be found in the fornix and on the plica itself. These penetrate into the underlying mesoderm and form *Krause's glands*.

Digitized by Illinois College of Optometry Library

There are three or four of them on the plica itself and of these one soon develops ahead of the others, and can be recognised as the so-called *Harderian gland* of the plica.

The Harderian gland is a racemose gland, occurring in many animals, but not in Primates, and opening by a duct deep to the plica semilunaris. It has a mucin-containing secretion.

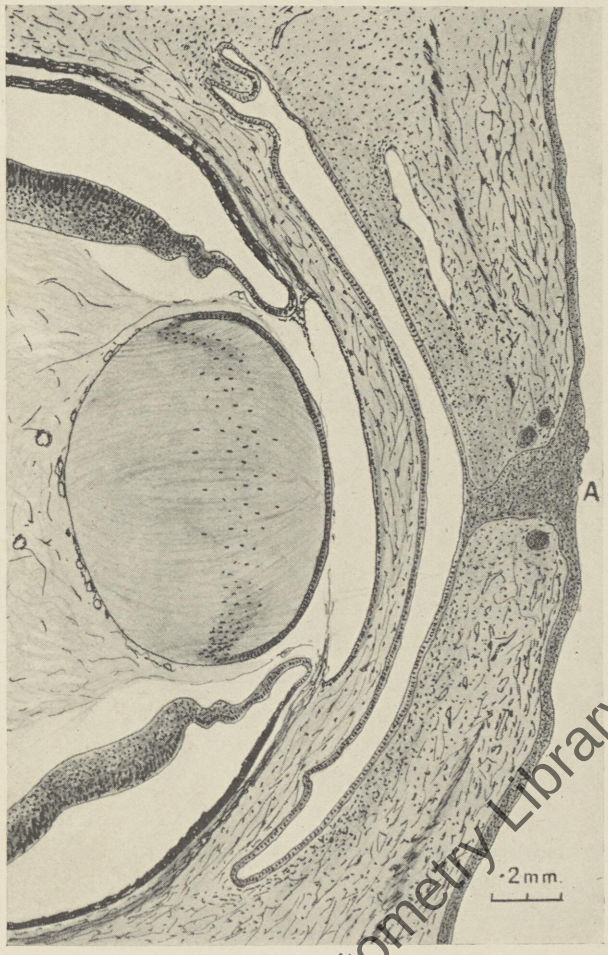


Fig. 226. Section through the fused lids of a 48 mm. human embryo. *A*, area of epithelial adhesion.

At the same time hair bulbs begin to develop on the caruncle a little after their appearance on the lid margins. The Harderian gland increases in size and shews branching acini and goblet cells by the 7th month. It regresses somewhat after this. The papillary folds in the fornices and the adenoid tissue and crypts in the plica and caruncle do not appear until immediately after birth.

Digitized by Illinois College of Optometry Library

The **lacrimal gland** begins its formation some little time after (about 25 mm.) the upper and lower canaliculi have been produced (18 mm.), in the shape of some half a dozen solid outgrowths from the upper and outer part of the conjunctival sac. Additional outgrowths are added to these throughout the 3rd month, and a set of branching

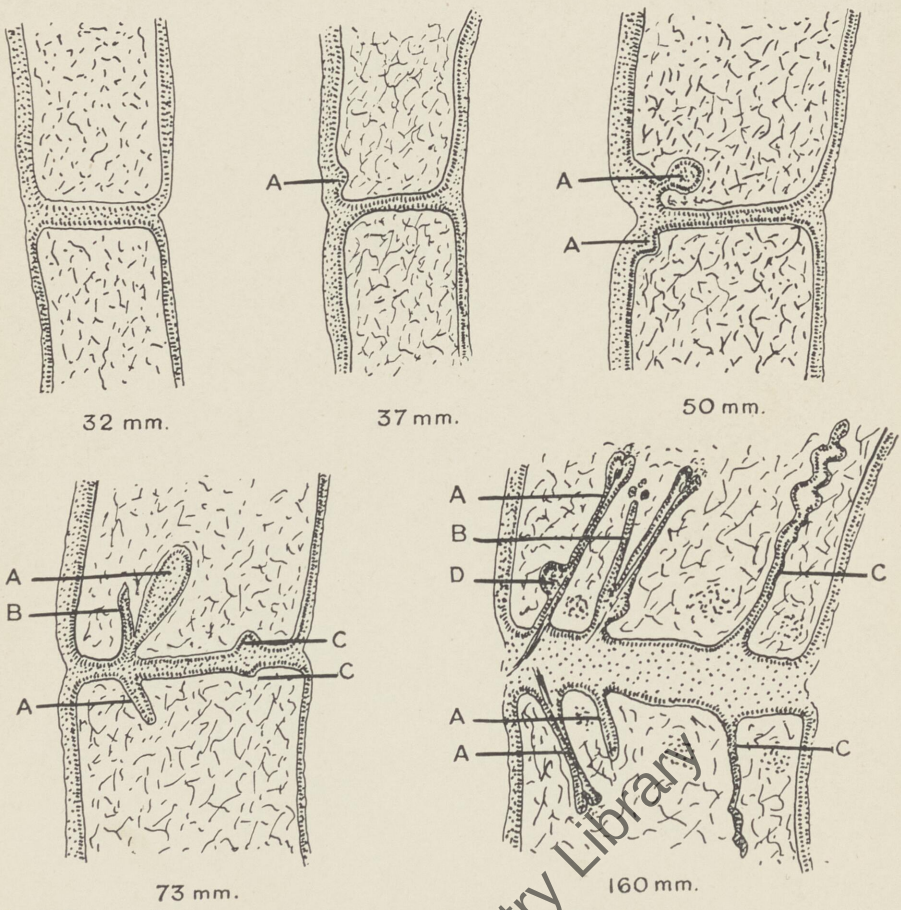


Fig. 227. Semi-diagrammatic sections through the fused lids of human embryos of 32, 37, 50, 73 and 160 mm. respectively. *A*, developing lash follicle; *B*, gland of Moll developing; *C*, Meibomian gland developing; *D*, gland of Zeiss developing.

tubules with large celled acini is thus produced. The gland is small at birth, growing during the first few years after birth, with change in its character, the lumina increasing in size and the intervening connective tissue stroma becoming much thicker.

The *differentiation of the lids* themselves has been worked out in detail by Contino, whose conclusions can conveniently be summarised here. At 37 mm., by which time epithelial adhesion between the lids is complete, the hair bulbs of the upper eyelashes are

Digitized by Illinois College of Optometry Library

beginning to develop. They form at first as little epithelial pits just at the outer angle of the lid margin. These pits deepen and a cylindrical downgrowth of surface ectoderm into the underlying mesoderm appears. This becomes differentiated into a hair bulb and hair in the same way as hairs are formed from surface ectoderm elsewhere. The lower lashes begin to appear at 40 mm. almost immediately after the upper ones, but throughout differentiation the lower lid always shews a distinctly less advanced stage than the upper. Fig. 226 shews a section through the fused lids of a 48 mm. human embryo in which both upper and lower lash follicles are apparent.

At 73 mm. the earliest signs of the *Meibomian glands* can be seen. These appear first as shallow depressions on the fused portion of the lid margin just in front of the posterior lid angle. At the same time small outpouchings of the walls of the follicles of the cilia can be found. These are the beginnings of the ducts of the *glands of Moll*. The acini appear rather later. By 90 mm. definite hair shafts can be seen in the ciliary follicles and a fresh series of buds begins from the walls of the follicles to form the *glands of Zeiss*. At the same time the Meibomian acini commence to form. Fig. 227 shews the principal stages of lid differentiation.

By the end of the 5th month the epithelial adhesion between the lids begins to break down, presumably by imbibition of sebaceous secretion from the glands, which leads to softening and disintegration of the cells.

According to Contino, the eyelashes are shed and replaced twice during intra-uterine life, once during the first half of the 7th month and again at the end of the 7th month.

C. The Position of the Eyes.

The alteration of the optic axes during ontogeny and phylogeny has already been touched on (p. 42). It remains to trace in the human embryo the stages of growth of the maxillary process which are correlated with this alteration.

At the 7–9 mm. stage the angle between the optic axes is 160°, and a section passing horizontally through both optic cups and their stalks will shew the disposition of parts seen in Fig. 228 *A*. The neural ectoderm of the eye and brain is shewn in black. These structures are entirely surrounded by and embedded in paraxial mesoderm. Immediately behind the eye lies the Gasserian ganglion, which is separated from the surface ectoderm by a thin layer of mesoderm. The ganglion, together with the carotid artery and the

Digitized by Illinois College of Optometry Library

cavernous sinus, which lie internal to it, just deep to the plane of section, is also entirely embedded within the paraxial mesoderm. They are, however, only separated below by a very thin layer of this from the supporting shelf of maxillary (visceral) mesoderm which lies behind and below the eye at this stage. Fig. 229 shews the relations of the eye and the maxillary process as seen from the surface in a 4·5 mm. embryo.

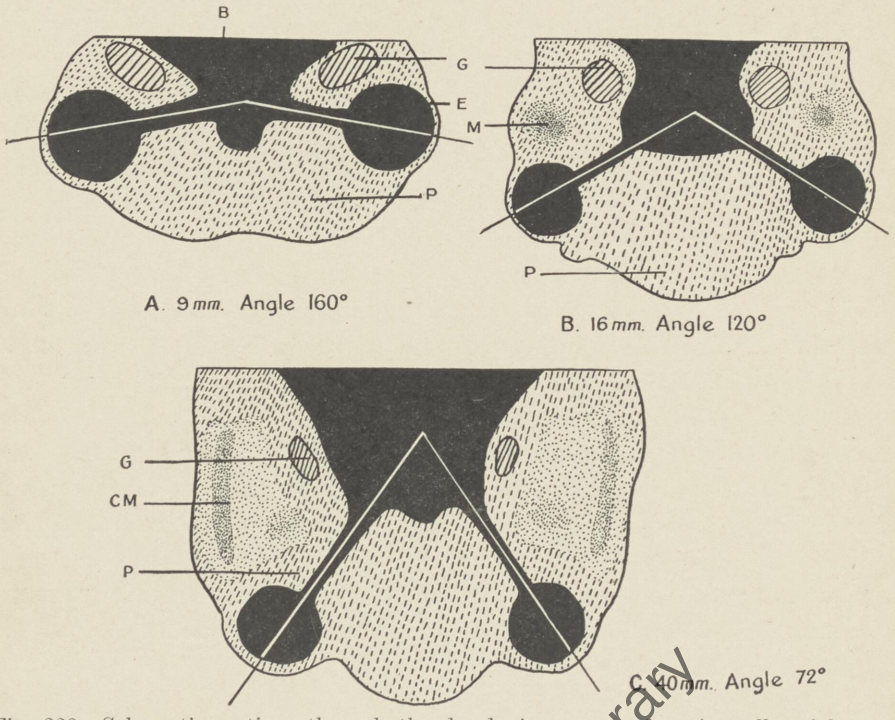


Fig. 228. Schematic sections through the developing eyes and optic stalks of human embryos of various stages. *A*, 9 mm. embryo. *B*, 16 mm. embryo. *C*, 40 mm. embryo. The decrease in the angle between the optic axes is apparent. B, brain; E, eye; P, paraxial mesoderm; M, maxillary mesoderm; G, Gasserian ganglion; CM, temporal condensation in maxillary mesoderm.

Fig. 230 shews the distinction between the visceral and paraxial mesoderm in the region of the eye. The section passes through part of the forebrain, the eye and the maxillary process of a 5 mm. human embryo. This disposition of parts can be realised better by considering the appearance of a section in a plane at right angles to that of the section in Fig. 228 *A* and passing through the Gasserian ganglion just behind the eye. This is shewn in Fig. 231 *A* at a slightly younger stage (7 mm.). The ganglion is seen in section near the surface, with the cavernous sinus on its inner lower aspect and the carotid artery internal to this again. These three structures lie

Digitized by Illinois College of Optometry Library

in paraxial mesoderm, supported on the maxillary process, which can be seen in section below them.

Soon after the 10 mm. stage the mesoderm of the maxillary process begins to extend in an upward direction between the Gasserian ganglion and the surface ectoderm, so that the ganglion comes to lie more deeply, and by the 16 mm. stage is separated from the surface both by a thin layer of the paraxial mesoderm in which it is embedded and by a wedge-shaped process of visceral mesoderm which now intervenes between it and the surface. This condition of things is seen in Fig. 231 *B*, which shews a section (in the same plane as Fig. 231 *A*) at the 16 mm. stage. The ganglion and the two vessels bear the same relation to each other as they did in Fig. 231 *A*, but the maxillary process has increased in extent. Within this growing visceral mesoderm two condensations can now be recognised. The one lying below the Gasserian ganglion is the beginning of the ali-sphenoid, the other, further out, further back and higher up, represents the rudiment of the tempora muscle and probably the squama temporalis. It is obvious that, at this stage, a horizontal section passing through the Gasserian ganglion, the eye and the optic stalk will also pass through the apex of the upward growing maxillary wedge. This apex now intervenes between the eye and the ganglion and, as a correlate of this increase in the structures behind the eye, the optic axes will be found to have become slightly more approximated, so that the angle between them is now only 120°. These relations are seen in Fig. 228 *B*, which shews such a horizontal section in a 16 mm. human embryo.

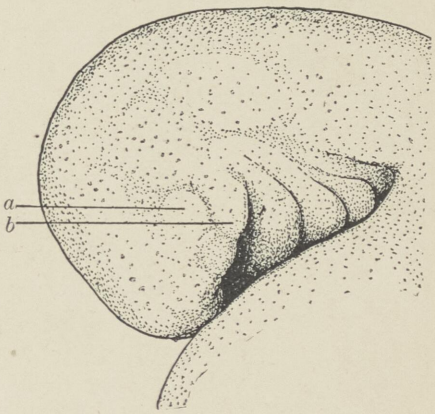


Fig. 229. Diagram shewing the side view of the head of a 4·5 mm. human embryo. The optic vesicle is situated at *a* and the maxillary process at *b*.

The upward-growing wedge of maxillary mesoderm increases in height and width, and the temporal condensations in it become more marked. As it increases, the Gasserian ganglion naturally appears to sink more and more deeply from the surface. Since the increase is in an antero-posterior direction as well as vertically, the eye and the ganglion also appear to become displaced with regard to each other, the former apparently swinging forward, with the result that the angle between the optic axes becomes still smaller, and the distance

Digitized by Illinois College of Optometry Library

between the eye and the ganglion both relatively and absolutely greater.

By 35 mm. a downward prolongation of the ali-sphenoid condensation can be recognised as the precursor of the external pterygoid

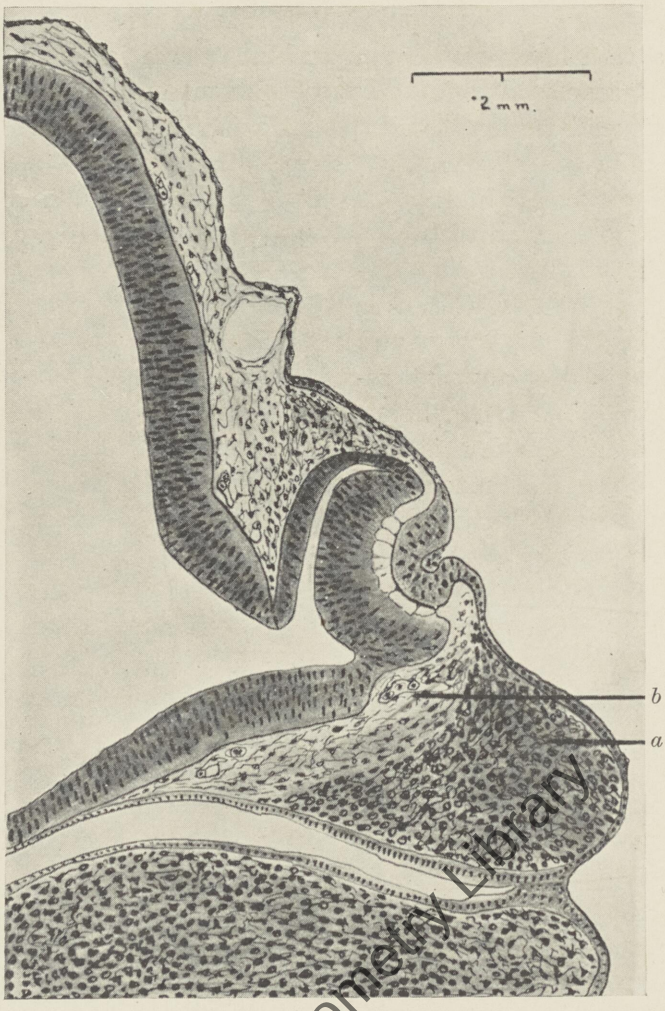


Fig. 230. Transverse section through the optic vesicle and maxillary process of a 5 mm. human embryo. *a*, "visceral" mesoderm of maxillary process; *b*, paraxial mesoderm.

plate, while the paraxial mesoderm in the middle line also shews signs of specialising into the basi-sphenoid. Fig. 231 *C* shews a vertical section through the Gasserian region comparable with that in Fig. 231 *A* and *B*. The ganglion, cavernous sinus and internal carotid artery are seen to lie as before, embedded in paraxial mesoderm, while the wedge of maxillary mesoderm outside them has

Digitized by Illinois College of Optometry Library

extended upwards to a marked degree. By 40 mm. the maxillary wedge has increased sufficiently to allow of the reduction of the angle between the optic axes to 72° (only about 10° greater than the adult angle). Fig. 228 *C* shews a horizontal section at the 40 mm. stage. The increase in size of the maxillary wedge is apparent. After this stage the process

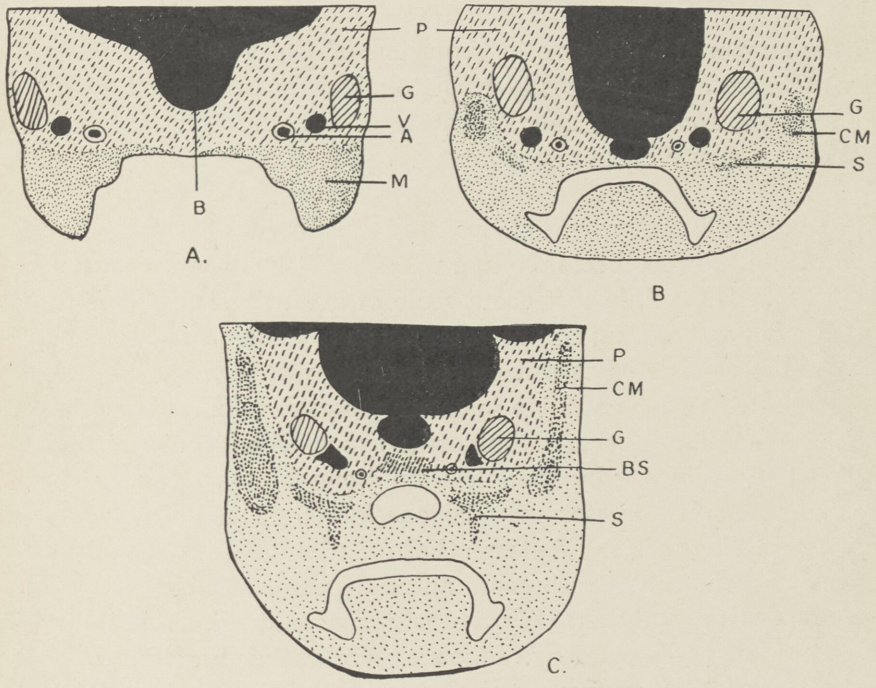


Fig. 231. Schematic sections in a plane passing through the Gasserian ganglion at right angles to the plane of section of the figures seen in Fig. 228. *A*, 7 mm. stage. *B*, 16 mm. stage. *C*, 35 mm. stage. P, paraxial mesoderm; G, Gasserian ganglion; V, cavernous sinus; A, carotid artery; M, maxillary process; B, fore-brain; CM, temporal condensation in maxillary mesoderm; S, ali-sphenoid condensation in maxillary mesoderm; BS, basi-sphenoid condensation in paraxial mesoderm.

is continued for a short time at a rapidly decreasing rate, the final angle between the optic axes being slightly variable but usually in the neighbourhood of 60°.

The **bony walls of the orbit** are formed from condensations in both maxillary and visceral mesoderm. The inferior and outer walls, as we have seen, are maxillary, the inner and upper, paraxial.

Digitized by Illinois College of Optometry Library

VIII

THE PHYLOGENETIC DEVELOPMENT AND MORPHOLOGY OF THE HUMAN EYE

The supposed phylogenetic evolution of the vertebrate from the invertebrate eye has already been touched on in Section I and, in view of the somewhat nebulous state of our knowledge of the link between the vertebrates and lower forms, need not be dealt with further.

There are, however, certain points in the evolution of the human eye within the vertebrate phylum which must be discussed at greater length. It is possible to trace a scale of evolution, both among the mammalia and among the vertebrates as a whole. When the entire phylum is considered it will be seen that, although the human eye represents the highest point in mammalian development, it is only one of a small number of culminating types, which have arisen from a common beginning by specialisation along diverging lines.

The common ancestor may be considered to have possessed an eye resembling in many features that found among the Ganoid fishes at the present time, since these animals possess an eye of a simple generalised type not shewing any of the modifications which might be considered as secondary. Like all vertebrate eyes, it is developed from *neural* and *surface ectoderm*, and is surrounded by *paraxial mesoderm*. The early stages of development (outgrowth of an optic vesicle from the fore-brain, invagination to form an optic cup, appearance of a lens thickening and lens vesicle, etc.) are similar to those found in any vertebrate, but there is no "abbreviation," and, in consequence, development can be more minutely studied. For example, the formation of the extrinsic muscles from the walls of the head cavities can be directly demonstrated. Some of the points in which the development of such an eye differs from the human type are as follows:

1. The growth of the lower part of the optic cup and the closure of the fissure are delayed until relatively late.
2. The hyaloid blood system is extremely rudimentary, and the hyaloid artery does not reach the lens.
3. The lens thickening is bi-convex in form and symmetrical.
4. The lens remains spherical.
5. No retinal vessels or macula lutea are developed.

Digitized by Illinois College of Optometry Library

6. The percipient elements of the retina are less crowded together, though their stages of differentiation are exactly similar to those found in man.

Such an eye contains the potentiality of specialisation along various lines, and we find examples of such specialisation among various groups of animals.

In the Mammalia the chief modifications of the basal plan lie in:

1. The early closure and obliteration of the fissure (and hence the absence of any specialisations connected with it) with the consequent earlier growth of the lower part of the cup.

2. The very complete development of the intra-ocular blood supply, both foetal and definitive.

3. A modification in shape of the lens plate (thicker in its inferior portion) and a gradual change in shape (throughout the order) of the adult lens from spherical to bi-convex.

4. A greater crowding together of the percipient elements, and the development in the highest Mammalia of an area of more acute vision, the macula lutea.

These modifications reach their acme of development in Man and the Anthropoids, but here and there on the upgrade within the Mammalia are found individual specialisations representing culminating points in different genera. As an example may be mentioned the development of the *tapetum* in Carnivores, and of the *mammillation* of the retina and choroid in Cheiroptera; no trace of either can be found in the Primates.

The human eye cannot be considered as reaching the high water mark of efficiency as an optical instrument, though the coincident development of the associated cerebral centres in man has given it undoubted precedence as a percipient organ.

In birds, evolution of the eye has proceeded along slightly different lines, and has resulted in the production of a more perfect optical mechanism, subserving a sense which plays an even greater part in the life of the bird than it does in man. This, however, is more than counterbalanced by the failure of coincident cortical development. In birds (and to a lesser extent in reptiles to which they are more closely allied than to mammals) the chief developmental departures from the basal type of vertebrate eye are as follows:

1. There is no tendency towards early disappearance of the fissure; correlated with this are found various specialisations which arise as elaborations of the fissural region. The chief among these are the *cauda* of the *optic nerve* and the *pecten*. The presence of these modifies considerably the development and the final appearance of the region

Digitized by Illinois College of Optometry Library

of the optic disc. The *cauda* is a drawn out portion of the optic nerve on the back of the eye, developed in a portion of the inner layer of the optic cup which becomes everted along the fissure, while the *pecten* is a bunch of capillaries covered by a thin sheath of neural ectoderm and projecting into the vitreous from the optic disc. Neither

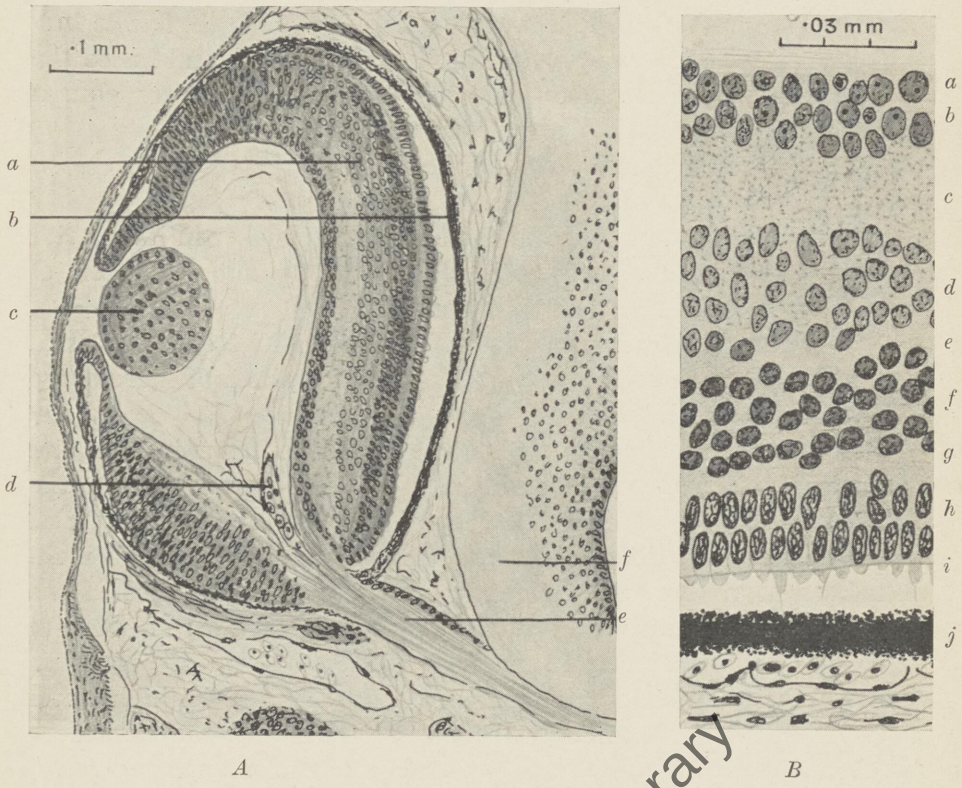


Fig. 232. *A*, section through the developing eye of the ganoid fish, *Amia calva* (the American Bow-fin). *a*, inner layer of optic cup, which is differentiating in the same way as the human retina, by the passage of cells from the outer towards the inner layers; *b*, outer pigmented layer of optic cup; *c*, spherical lens; *d*, hyaloid artery, which does not form a tunica vasculosa lentis; *e*, optic stalk containing nerve fibres; *f*, fore-brain. *B*, section through a portion of the retina of the above. *a*, nerve fibre layer; *b*, layer of ganglion cells; *c*, inner molecular layer; *d*, layer of amacrine cells; *e*, transient fibre layer of Chievitz; *f*, layer of bi-polar cells; *g*, outer molecular layer; *h*, layer of rod and cone nuclei; *i*, rods and cones; *j*, pigment epithelium.

of these structures is present in the Mammalia, though the rudiments of which they are the elaborations can sometimes be recognised in early embryonic stages.

2. The lens shews a specialised structure, the *annular pad*, which is peculiar to the Sauropsida. It is formed at the equator by elongated cells of the lens epithelium.

3. The retina shews a high grade of specialisation. The *macula* is present and may assume (in birds) complicated forms (e.g. it may

Digitized by Illinois College of Optometry Library

be double or spread out into a long band) quite unlike anything found in any other order. The rods and cones shew globules of a highly refractile coloured material not so far known to be present in any of the mammals or fish.

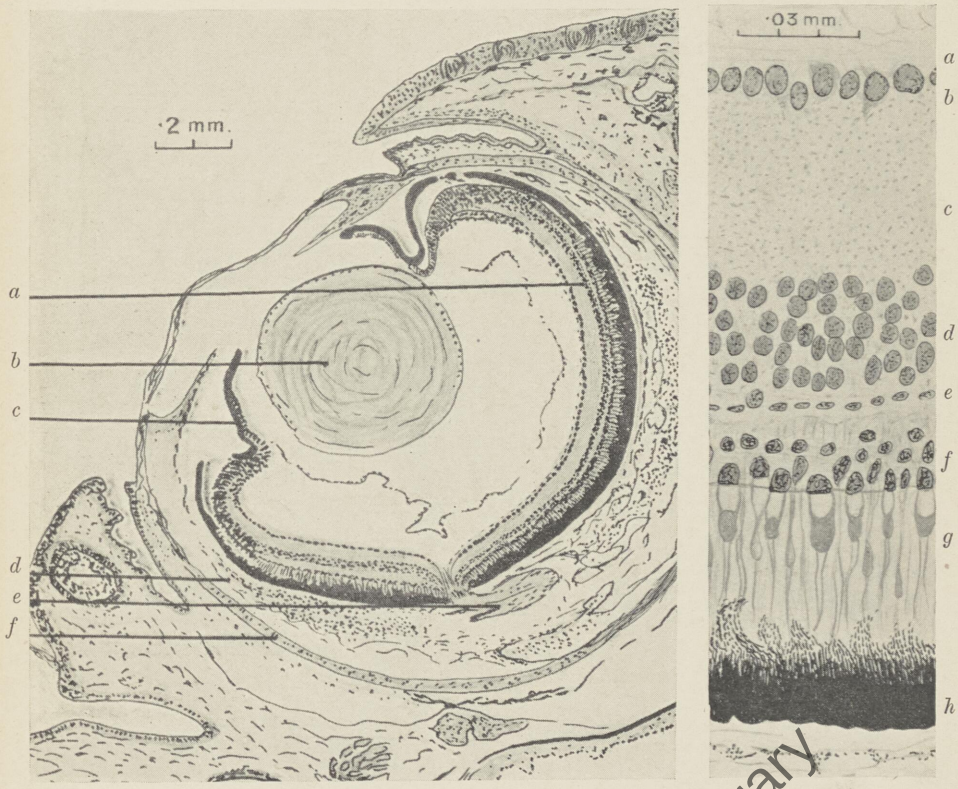


Fig. 233. *A*, section through the developing eye of the Ganoid *Amia calva*—more advanced stage than that in Fig. 232. *a*, retina, almost completely differentiated; *b*, spherical lens, without vascular capsule; *c*, iris developing from margin of optic cup; *d*, choroid; *e*, optic nerve; *f*, sclerotic becoming cartilaginous. *B*, section through the retina of the above. *a*, nerve fibre layer; *b*, layer of ganglion cells; *c*, inner molecular layer; *d*, layer of amacrine and bi-polar cells; *e*, layer of horizontal cells; *f*, nuclei of rods and cones; *g*, rods and cones, shewing high grade of development, but relatively large size and sparse arrangement; *h*, pigment epithelium with processes passing between the outer limbs of the rods and cones, a characteristic of the retina of the lower vertebrates.

As in the primitive type, the hyaloid blood system remains extremely rudimentary and no tunica vasculosa lentis or direct retinal blood supply is formed. This is an advantage from an optical point of view, since there are no foetal remains in the vitreous and no circulating blood corpuscles in front of the rods and cones to interfere with their function.

Digitized by Illinois College of Optometry Library

The whole eye is relatively much larger and more conspicuous in the Sauropsidan embryo than in any other vertebrate.

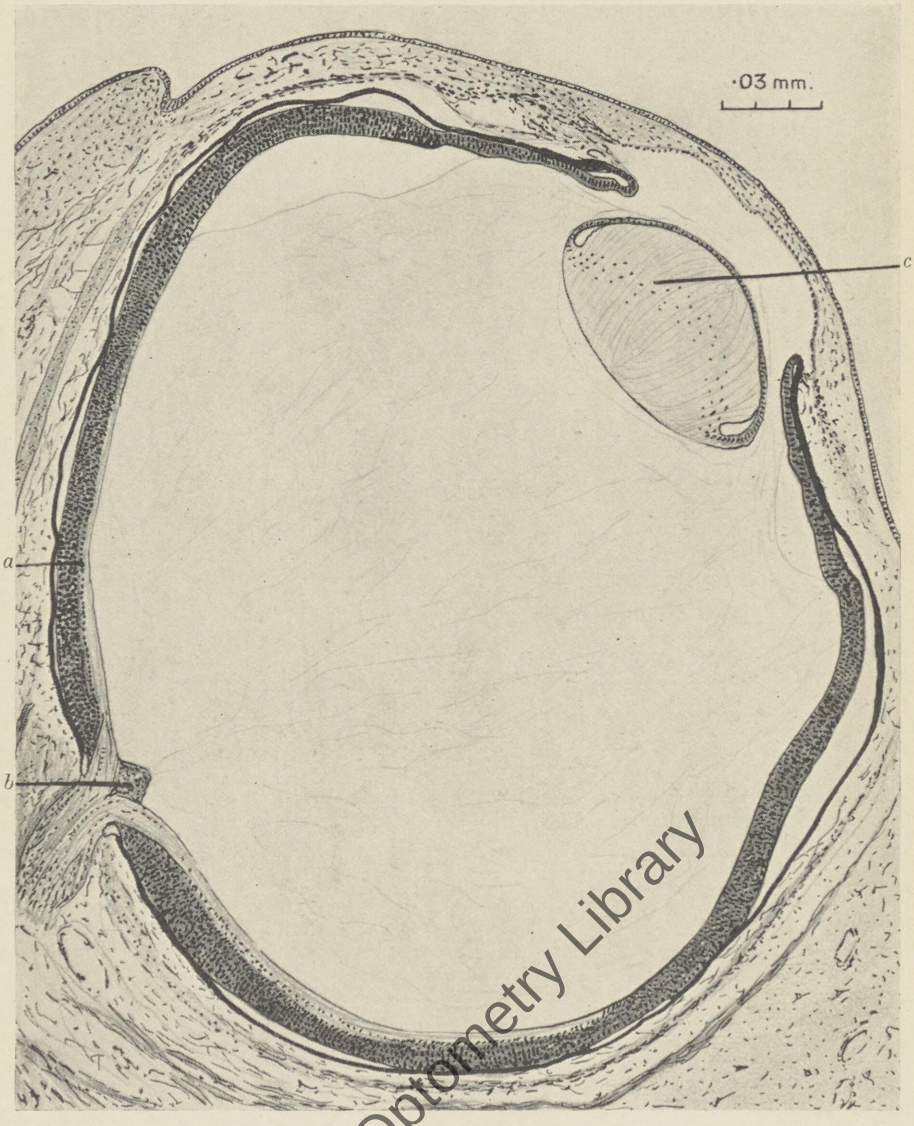
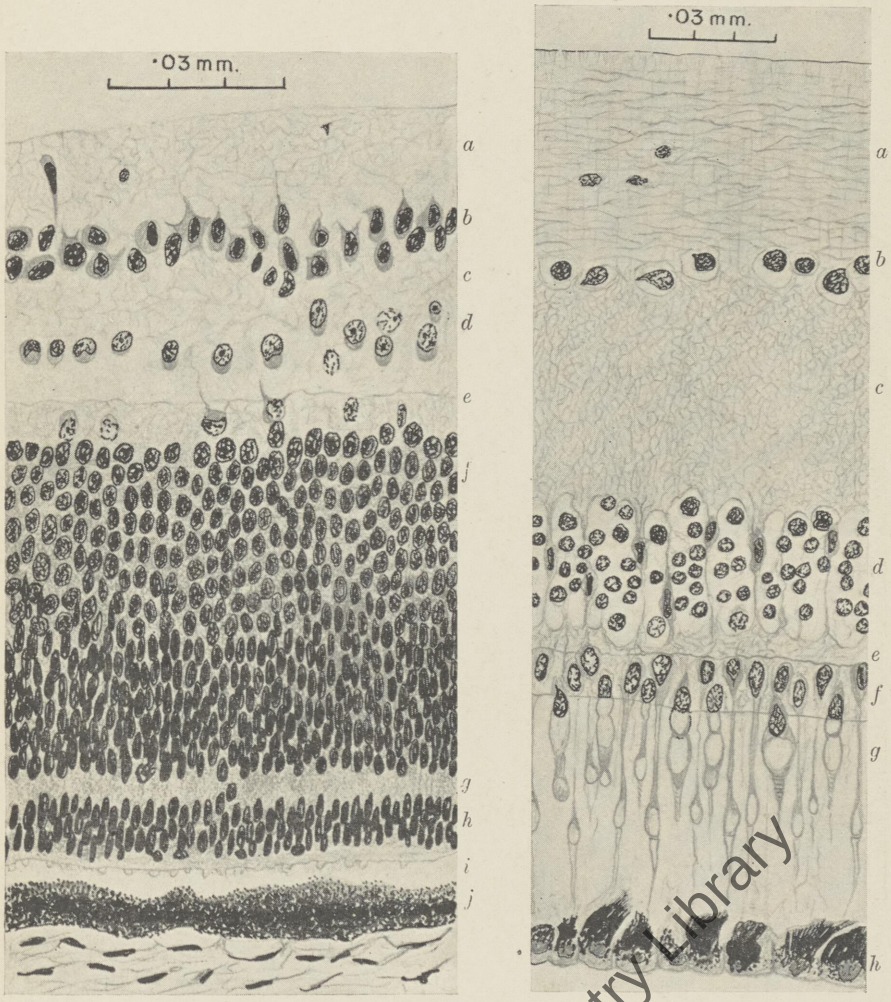


Fig. 234. Section through the eye of a developing chick. *a*, inner layer of optic cup differentiating to form retina; *b*, optic disc shewing specialisation of Bergmeister's papilla to form the rudiment of the pecten which later grows out into the vitreous; *c*, lens, which is bi-convex and shews the beginning of the annular pad in the equatorial region.

The Sauropsida, culminating in the birds, have therefore evolved a highly efficient eye by increase in size and by elaboration of the cleft region, the hyaloid blood system remaining rudimentary, while,

Digitized by Illinois College of Optometry Library

on the other hand, the Mammalia have elaborated the hyaloid system and, if anything, slightly reduced the size, but since both lines of



A B

Fig. 235. Sections through the retina of the chick shewing similar differentiation to that found in all the other vertebrates. *A*, developing chick. *a*, nerve fibre layer; *b*, ganglion cell layer; *c*, inner molecular layer; *d*, amacrine cells; *e*, fibre layer of Chievitz (exceptionally well developed in birds); *f*, bi-polar cells not yet all differentiated; *g*, outer molecular layer; *h*, rod and cone nuclei; *i*, rudimentary rods and cones; *j*, pigment epithelium, which has no processes as yet. *B*, definitive retina of chick. *a*, nerve fibre layer; *b*, ganglion cell layer; *c*, inner molecular layer; *d*, bi-polar layer formed by fusion of *d*, *e* and *f* in 235 *A*; *e*, outer molecular layer; *f*, nuclei of rods and cones; *g*, rods and cones. Note large size and high degree of specialisation; *h*, pigment epithelium, which now shews processes passing inwards.

development have ended in the production of a macula, both shew a final high grade of functional efficiency, though it was reached along diverging lines.

Digitized by Illinois College of Optometry Library

Figs. 232, 233, 234 and 235 shew examples of embryonic stages in a Ganoid fish and in a bird. The legends are self-explanatory.

Apart from these differences of shape, size and blood supply arising during evolution, there is a definite and steady tendency towards

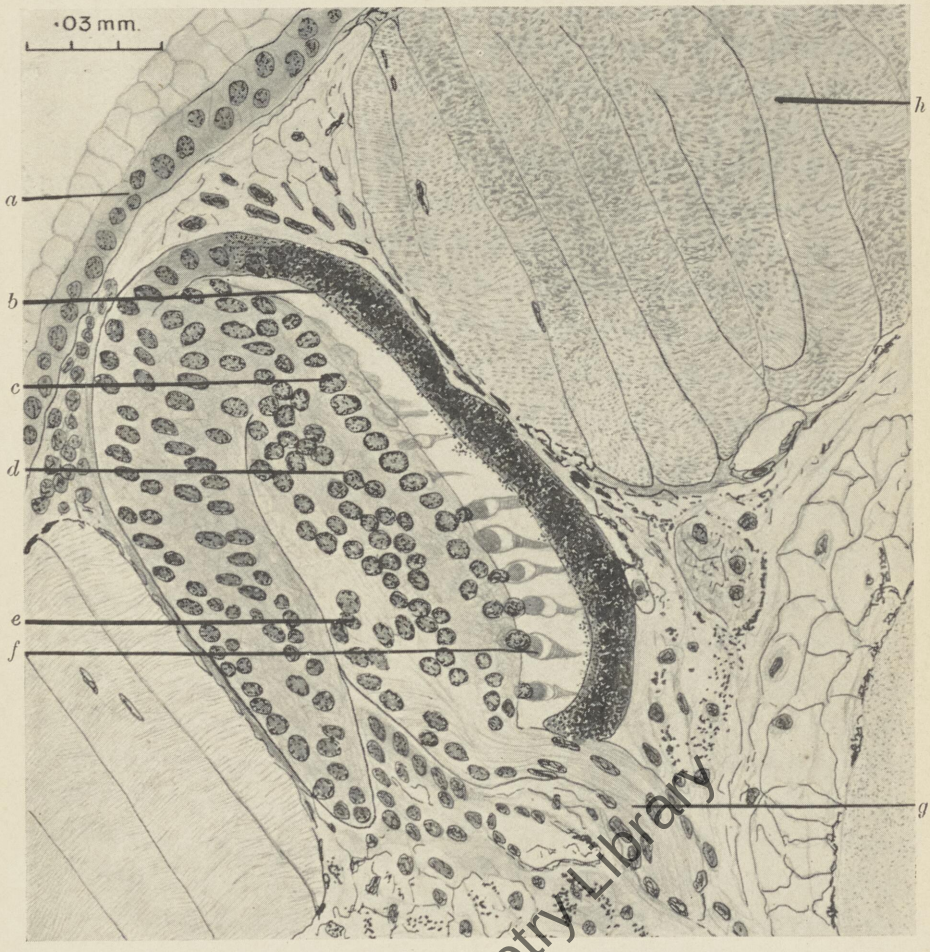


Fig. 236. Section through the developing eye of *Petromyzon fluviatilis* (larval lamprey). The optic cup is closely folded together, there is no vitreous and no lens, but the outer layer of the cup is pigmented and the inner layer shews advanced differentiation. *a*, surface epithelium of head; *b*, outer layer of optic cup; *c*, nuclei of rods and cones; *d*, nuclei of bi-polar cells; *e*, ganglion cells with nerve fibres arising from them; *f*, percipient element (there is one sort only of these and they cannot be distinguished as either rods or cones); *g*, optic nerve; *h*, muscle of head.

modification of *retinal histology*. This tendency is always in the direction of increase in number of percipient elements in a given retinal area. This is obviously correlated with an increase in visual acuity, since it means an increase in the number of points on an object which can be perceived as separate. The highest known concen-

Digitized by Illinois College of Optometry Library

tration of cones is seen in the human macula. Fig. 236 shews the developing eye of one of the lowest known vertebrates, *Petromyzon fluviatilis*. This animal, the lamprey, belongs to the Cyclostomata, and in many respects approximates to an invertebrate type. It will be seen that the percipient elements of the retina are very large and that there are gaps between them. It can be ascertained by measurement that the number of them present in 0·01 sq. mm. is only 100. If now the same measurement is made on an amphibian eye (for example, the frog shewn in Fig. 237) the number in 0·01 sq. mm. will have increased to 125. Passing higher in the scale, we find a large increase among the Sauropsida, up to 330 even in regions outside the macula. In the macula in man the figure reached is approximately 625 or more, thus shewing that this increase is definite and continuous, and not influenced necessarily by accompanying modifications.

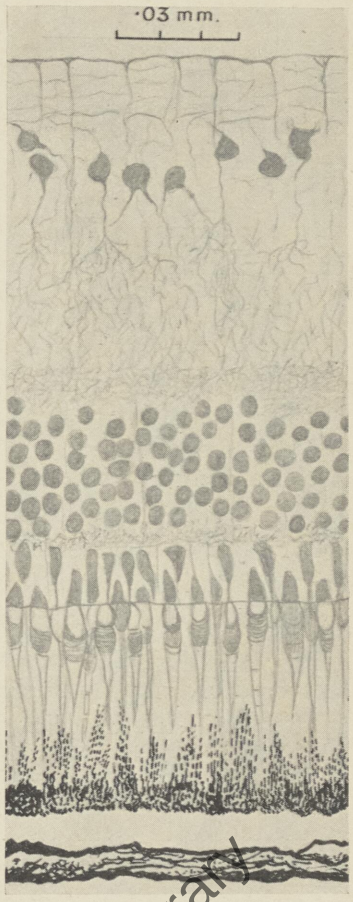


Fig. 237. Section through the retina of a frog. The general arrangement in layers is that found in all vertebrates. The percipient elements are more crowded together than those in Fig. 236 and slightly less than those in Fig. 235 *B*.

The Comparison of the Retina with other Ectodermal Derivatives

A point in the morphology of the retina which remains to be discussed is its comparison with other ectodermal derivatives. Numerous attempts (Loewe, Merk, *inter alia*) have been made to homologise the layers of the skin, the cerebral cortex and the retina. The comparison given by Merk may be quoted here:

Eye	Central nervous system	Skin
Outer limbs, rods and cones	Ependyma	Stratum corneum
Inner ,, ,, ,,	Ganglandic layer	,, lucidum
Outer molecular layer and the rest of the retina	Outer cell strata	,, Malpighii
Internal limiting membrane	Pia and arachnoid interna	—

He states that the comparison cannot be made to include the three retinal layers in detail as they are not represented in the brain. This

Digitized by Illinois College of Optometry Library

comparison is open to certain grave objections. In the first place, the comparison is made between the adult stages of skin, retina and cerebral cortex. By this time extreme specialisation has occurred so that most traces of original similarity have been lost and the comparison appears at best somewhat strained. If any similarity is to be observed it will be in embryonic stages. In the second place, it is doubtful whether an analogy of any value can ever be drawn between the skin and the cerebral cortex. The separation of ectoderm into neural and surface ectoderm appears so fundamental and to have arisen so early (i.e. long before the vertebrate phylum) that it is doubtful whether one is justified in seeking to compare them. The essential difference in the position of the respective proliferating layers alone makes the task an extremely difficult one. In the skin the layer of nuclei which remain unspecialised for purposes of reproduction (palisade layer) and by the division of which all the other layers are formed, is to be found on the deep aspect of the epithelium, i.e. on the side in contact with mesoderm. The cornification of the outer layer of the skin is a sign of death of the cells and is associated with constant frictional loss and replacement from the deepest layers. In the walls of the central nervous system, however, the proliferating layer, i.e. that from which the other layers are formed, is that immediately on the surface towards the cavity of the central nervous system, which surface represents the original surface of the body. The cells produced by this proliferating layer form the layers of the wall of the central nervous system of which the outermost one lies in contact with mesoderm. The cells do not cornify nor become cast off and it appears impossible to consider the two cases as parallel. Even if one does not consider the mode of growth of the two, and merely tries to homologise the stratum corneum of the adult skin with the cilia of the ependyma of the central nervous system, the parallel still breaks down, since the cilia are appendages of the cells of the ependyma, while the stratum corneum is composed of transformed cells themselves. Hence one cannot with justice homologise either the layer of cilia with the stratum corneum or the layer of rods and cones with the stratum corneum. It seems, therefore, wiser to abandon the attempt to include surface ectodermal derivatives in the same category as neural. It is, on the other hand, a comparatively easy task (once the question of the skin has been set aside) to draw a parallel between all the structures derived from the wall of the neural tube. It is in early stages of development alone, however, that the homology can be successfully demonstrated.

The wall of the cerebral vesicle (and earlier of the spinal cord also),

Digitized by Illinois College of Optometry Library

like that of the optic vesicle, consists at first of a simple neuro-epithelium. It soon, like the inner layer of the optic vesicle, develops a clear marginal zone and a nucleated mantle zone, the deepest nuclear row of which shews mitoses and forms the ependymal or

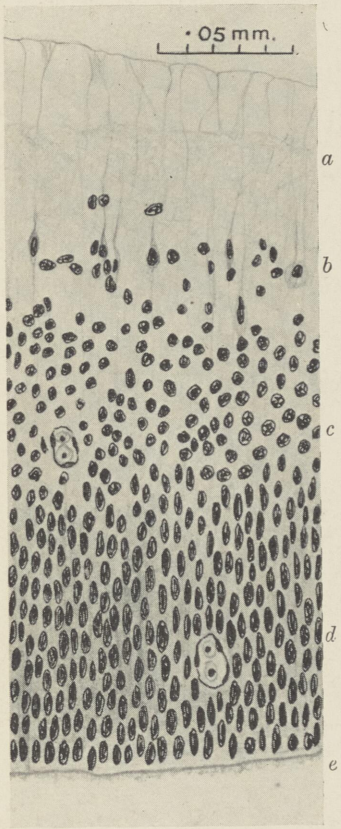


Fig. 238. Section through the wall of the fore-brain of a 12 mm. human embryo. *a*, marginal layer with glial fibres forming an internal limiting membrane; *b*, migrating round cells and nuclei of glial fibres; *c*, layer of differentiating round cells; *d*, proliferating layers; *e*, layer of cilia.

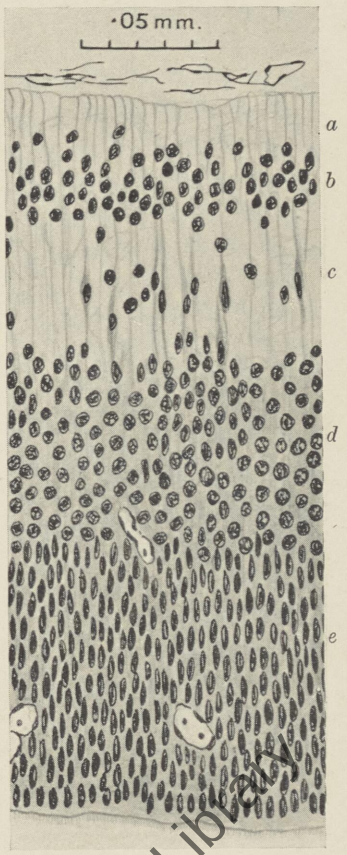


Fig. 239. Section through the wall of the cerebral vesicle of a 25 mm. human embryo. *a*, marginal layer; *b*, layer comparable with ganglion cell layer of developing retina; *c*, glial nuclei and migrating cells; *d*, layer of round nuclei; *e*, layer of oval nuclei.

proliferating layer. In the cortex, as in the retina (and also in the spinal cord), the next stage is the appearance of the supporting tissue. In the marginal zone definite glial fibres (looking exactly like developing fibres of Müller) make their appearance, their processes run towards the outer surface of the cortex, where they end in anastomosing foot-plates and form a limiting membrane exactly like

Digitized by Illinois College of Optometry Library

the internal limiting membrane in the eye (see Figs. 67, 71 and 73 for comparison). These glial fibres have oval nuclei which can be seen forming the beginnings of a second layer of nuclei in Fig. 238. Among them are cells with round nuclei, evidently derived from the layer of round nuclei below. These round nuclei can be compared with the developing ganglion cells in the retina. Figs. 67 and 71

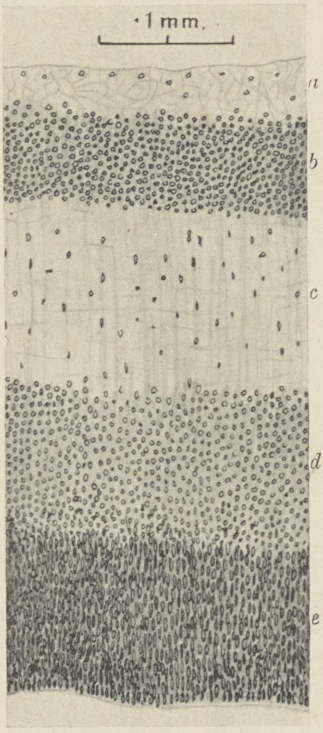


Fig. 240. Section through the wall of the cerebral vesicle of a 48 mm. human embryo. *a*, outer fibre layer; *b*, outer cell layer; *c*, middle fibre layer; *d*, middle cell layer; *e*, inner cell layer.

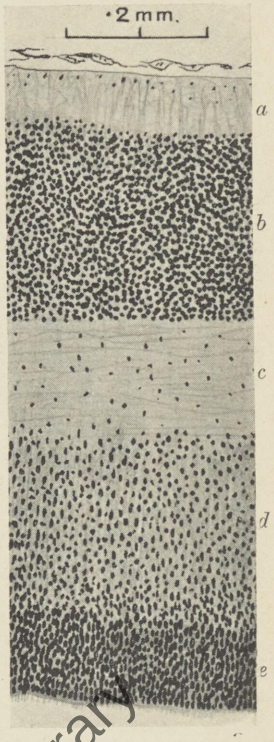


Fig. 241. Section through the cerebral cortex of a 75 mm. human embryo. *a*, outer fibre layer; *b*, outer cell layer; *c*, middle fibre layer; *d*, middle cell layer; *e*, inner cell layer.

(from a 12 mm. and a 17 mm. human embryo) shew the migration (in the retina) of ganglion cells and fibres of Müller, while Fig. 238 shews an exactly similar process going on in the wall of the fore-brain of the same 12 mm. human embryo. By 25 mm. (Fig. 239) the separation of the nuclei of the supporting fibres from the ganglion cells in the wall of the brain has become more marked, and resembles the stage of retinal development seen in Fig. 75 (48 mm.). The underlying layers in the cortex are composed of round nuclei (outermost 8–10 rows) and oval nuclei (inner 10–12 rows). This is apparent

Digitized by Illinois College of Optometry Library

also in the retina in Fig. 75. The most important structural difference between retina and cortex is that the layer bounding the ependyma is composed of many very fine short cilia, while in the retina rods and cones are beginning to appear, farther apart and longer than the cilia. They bear, however, exactly the same relations to the cells of the proliferating layer as do the cilia.

Fig. 240 shews the cortex of a 48 mm. human embryo. The total thickness is much greater than in Fig. 239 and the most superficial layer (comparable with the ganglion cell layer) now consists of 10–12 rows of nuclei. The interval between this layer and the layer of round nuclei beneath has increased enormously and contains still some nuclei of supporting fibres. The separation of the nuclei into three main bands is very clear and should be compared with that seen in the retina in Figs. 75, 77 and 80. The subsequent stages of differentiation of the cortex cause it to become more and more unlike the retina, so that the parallel should really cease at this, the 48 mm. stage. Thereafter in the retina the nerve fibre layer increases in thickness, the ganglion cell layer thins and the inner granular layer comes to equal the nerve fibre layer in width. In the cortex, on the other hand, the superficial layer of nerve fibres remains very thin, and the "ganglion cell" layer becomes extremely thick. In the cortex of a 75 mm. embryo (Fig. 241) this process is seen, so that the resemblance to the retina is much less than it was in the earlier stages. In subsequent stages the parallel cannot be successfully traced.

It can, therefore, with reason be said that a close analogy is possible between cortex and retina up to the 4th month of development. This analogy may be expressed thus:

Retina	Cortex at 4th month
Internal limiting membrane	Pia mater
Nerve fibre layer	Thin outer fibre layer
Layer of ganglion cells	Outer cell layer
Inner molecular layer	Inner fibre layer
Bi-polar layer	Middle cell layer
Outer molecular layer	Not represented at this stage
Nuclei of rods and cones	Inner cell layer
External limiting membrane	Basement membrane of ependyma
Rods and cones	Cilia

In addition we can find in the ependyma of the choroid plexuses a parallel for the pigment epithelium of the retina and ciliary processes. In amphibian brains this ependyma is often densely pigmented and resembles very closely the ciliary body—in human brains it is not pigmented, but it is a simple epithelium, similar to the pars ciliaris retinae even in the fact that it exercises a secretory function, if one

Digitized by Illinois College of Optometry Library

can consider the cerebro-spinal fluid as at all comparable with the aqueous humor.

That in spite of its relative simplicity of structure the human eye is capable of an extremely high degree of functional activity, probably surpassed only by that of the bird, is, however, undoubted. The factors which are responsible for this efficiency are three.

In the *first* place, there is a slow but definite and steady tendency throughout phylogeny towards an increase in the number of percipient elements in a given area, with consequent increase in possible power of discrimination.

In the *second* place, a tendency towards specialisation of areas of acute vision begins to appear above the reptiles, making possible on the one hand the elaborate arrangements of birds and on the other the macula lutea of man.

Thirdly, throughout phylogeny there has been a coincident elaboration of the central nervous system allowing of increasingly complex reactions to the stimuli received through the organs of the special senses.

This third factor is by far the most important in estimating the evolutionary reasons for the efficiency of the human eye, and it is safe to state that in the human eye we have perhaps the best example of the high grade of activity possible from the linking up of a fairly primitive sense organ with an extremely complex brain.

Digitized by Illinois College of Optometry Library

IX

SYNOPTIC COMPARISON OF OCULAR WITH GENERAL DEVELOPMENT

The development of the eye may be correlated with the development of the rest of the body by considering certain typical embryonic stages. In the following table the stages have been chosen as being each characterised by some important change in the condition of the eye: the stage of ocular development is contrasted with the stage of development of various other important organs in the body so that some idea may be gained of the inter-relation of developmental processes[1].

STAGES OF EMBRYONIC DEVELOPMENT

Length of embryo	Condition of eye	Condition of certain other important organs and of general body form
2·6 mm.	The optic pits are visible as depressions in the floor of the wide open neural plate.	The embryo has fourteen somites, and the remains of the primitive streak can still be seen. The notochord is developing, but is not yet free from entoderm in the cranial region. The medullary canal is closed in its central part only. The site of the auditory vesicle is marked by a thickened plate of ectoderm. The pharyngeal membrane is still intact. The first two branchial pouches reach the ectoderm, the third is just formed. The rudiments of the pronephros are appearing. The allantoic duct is present. A pair of aortae are present.
3·2 mm.	The optic pits have been converted into optic vesicles by the closure of the anterior end of the neural tube. The optic vesicles are in contact with the surface ectoderm which is beginning to thicken to form a lens plate.	Twenty-three somites are present and the primitive streak is no longer visible. The notochord is separated from entoderm throughout its whole length. Neuromeres can be recognised in the neural tube and the roof of the 4th ventricle is thinning. The auditory vesicles are beginning to constrict off from the ectoderm.

[1] The ages of appearance of most of the important organs are taken from the *Normentafel* of Keibel and Elze.

Digitized by Illinois College of Optometry Library

Length of embryo	Condition of eye	Condition of certain other important organs and of general body form
		The olfactory areas are visible and the placodes of the facial and glossopharyngeal nerves are formed. The rudiment of the hypophysis can be seen. The pharyngeal membrane has disappeared. The rudiments of the stomach and the dorsal pancreas can be recognised and there is a short tail gut.
4·5 mm.	The lens plate is more marked and the outer wall of the optic vesicle is thickening. Vascular mesoderm forming the first sign of the hyaloid artery is beginning to insinuate itself between the lens plate and the optic vesicle.	Thirty-five somites are present and seven neuromeres in the region of the 4th ventricle. The auditory vesicle is now completely separated from the surface and the ductus endolymphaticus is formed. The hypophyseal pouch is much broader. Four branchial pouches reach the ectoderm and the tuberculum impar and the rudiment of the median thyroid are apparent. The trachea is constricted off and the bronchial buds are apparent but undivided. The stomach rudiment is commencing to rotate. The gall bladder is formed and the ventral pancreas appearing. The mesonephros is present. The Wolffian ducts have reached the cloaca but have not yet opened into it. The metanephric buds are just visible. The limb buds are beginning.
5 mm.	The optic vesicle is beginning to invaginate to form the optic cup and the distinction between inner and outer walls of this is established. Pigment grains can be found in the outer wall and the primitive choroid is forming. The lens pit is appearing in the lens plate.	The general development is very little different from that of the 4·5 mm. stage described above.
7 mm.	The optic vesicle has fully invaginated, and the foetal fissure is recognisable and open throughout its whole	The cerebral hemispheres are present. In the spinal cord the anterior horns and the anterior and posterior columns are apparent. The placode

Digitized by Illinois College of Optometry Library

Length of embryo	Condition of eye	Condition of certain other important organs and of general body form
	length. The marginal zone of the retinal layer is well developed. The lens pit has deepened to form a lens vesicle, which is closed but is still in continuity with the surface ectoderm. The posterior part of the tunica vasculosa lentis is just beginning to form and is definite by the 9 mm. stage.	of the vagus has now appeared. The olfactory area is slightly depressed. Four branchial pouches reach the ectoderm and a fifth is beginning. The thyro-glossal duct is obliterated. The basal lingual and arytenoid swellings are present. The bronchi are giving off their first divisions. The rotation of the stomach is not yet complete. There is a simple intestinal loop and the caecum shews as a spindle shaped enlargement. The tail gut now extends from the cloaca to the tip of the tail. The Wolffian ducts open into the urogenital sinus after giving off the ureters. The rudiment of the cortex of the supra-renal body is present. The inferior vena cava is beginning. The skeleton is in the mesenchyme stage. The base of the skull, the pars petrosa, the vertebrae, the humerus, femur and some ribs are recognisable.
10 mm.	The pigment in the outer layer of the optic cup has increased considerably. The retinal layer still shews merely a division into a cellular and a marginal zone, but this stage ends the first period of retinal development. The foetal fissure is still open. The lens vesicle has separated from the surface ectoderm. Its cavity contains remains of epitrichial cells. The cells of its posterior wall are slightly elongated. The beginning of the lateral part of the tunica vasculosa lentis can be seen, and the annular vessel is developing. The optic axes make an angle of 160° with each other. The rudiment of the naso-lacrimal duct can be recognised.	Neuromeres can still be seen in the region of the 4th ventricle. The posterior commissure is formed. The semi-circular canals are present in the form of pouches only. The median thyroid has not yet reached the lateral thymus and the lateral thyroid is still connected with the pharynx. The bronchi have divided twice. The caecum and the vermiform appendix can be seen and scanty remains of the tail gut are still present. The pancreatic rudiments are almost in their final position. Rudiments of epithelial buds are present in the small intestine. The renal pelvis is present as a bud and the ureters open into the Wolffian ducts. The cloaca is not yet completely divided up. In the heart the septum primum and the foramen ovale are complete, but not the septum ventriculorum. The rudiment of the mammary gland can be seen. The base of the skull, the vertebrae, ribs, scapula, humerus, radius,

Digitized by Illinois College of Optometry Library

Length of embryo	Condition of eye	Condition of certain other important organs and of general body form
		ulna and femur are in the stage of pre-cartilage.
12 mm.	Beginning of second stage of retinal development. Migration of cells into the marginal layer to form the primitive inner nuclear layer can be seen. The foetal fissure is closing in its central part. The cells of the posterior wall of the lens vesicle are now forming primary lens fibres, which do not yet fill the cavity of the vesicle. The posterior and lateral portions of the tunica vasculosa lentis are more advanced. The lid folds are apparent.	General development similar to that of 10 mm. embryo described above.
13 mm.	The foetal fissure has closed except for a notch at the margin of the cup. The lens vesicle is almost filled by the primary lens fibres. The hyaline capsule of the lens has appeared. The membrane of Bruch is developing.	General development similar to that of the 10 mm. embryo described above.
17 mm.	The primitive inner nuclear layer of the retina is well formed at the posterior pole and nerve fibres can be traced from its cells along the optic stalk as far as its central end. The cavity of the lens vesicle is completely obliterated by the primary lens fibres. The anterior portion of the tunica vasculosa lentis is forming and the common ciliary arteries are present.	General development similar to that of the 10 mm. embryo described above.
18 mm.	The anterior chamber is just beginning to form.	General development similar to that of the 10 mm. embryo described above.
20 mm.	The nerve fibres now fill the inner layer of the optic stalk. The anterior cham-	The cochlea shews three-quarters of a turn. The auditory ossicles, the external ear and the meatus are

Digitized by Illinois College of Optometry Library

Length of embryo	Condition of eye	Condition of certain other important organs and of general body form
	ber is present as a completely closed space. The anterior portion of the tunica vasculosa lentis is more advanced. Vasa hyaloidea propria are present. The lid folds are growing over the eyes. The lacrimal canals are present but do not reach the surface. The optic chiasma is apparent.	cartilaginous. The epithelial rudiment of the external nares is present and the turbinals can be recognised. The palatal processes lie beside the tongue and the intrinsic lingual muscles are differentiated. Rudiments of teeth are present. The sub-maxillary gland has budded out well but not the parotid. The larynx is cartilaginous, the bronchi have divided eight times. Muscle is present in the walls of the oesophagus, stomach, duodenum and rectum. The anus is closed. A physiological umbilical hernia is present. The ventricular septum is complete. The sex can be recognised from the structure of the reproductive gland. The uro-genital sinus is open. The terminal phalanges of the great toes are cartilaginous. The humerus, femur, tibia, mandible, maxilla, pre-maxilla and palate are ossifying. The clavicle contains both bone and cartilage.
26 mm.	The secondary lens fibres begin to form immediately after this. The anterior vascular capsule of the lens is complete. Descemet's endothelium is differentiated. The lacrimal gland is recognisable. Hair rudiments can be seen in the region of the eyebrows.	The olfactory lobe is present. The choroid plexuses are enormously developed in the lateral and 4th ventricles. The medullary canal still extends to the coccygeal tubercle. The parotid gland is beginning. The lungs extend from the 2nd to the 9th thoracic vertebra. All the cardiac valves are formed. Circular muscle fibres are present throughout the whole intestine. The smooth muscle of the bladder is formed. The uro-genital sinus is open. There is sympathetic tissue in the centre of the supra-renal. Thirty-four vertebrae are present and the cartilaginous skeleton is complete. Bone is now present also in the fibula, radius, ulna, frontal, zygoma and squama temporalis.
35 mm.	The secondary lens fibres are appearing and the suturing of the inner embryonic nucleus can be seen. The tunica vasculosa	General development is very similar to that of the 26 mm. embryo described above.

Digitized by Illinois College of Optometry Library

Length of embryo	Condition of eye	Condition of certain other important organs and of general body form
	lentis and the vasa hyaloidea propria have reached the height of their development. The optic stalk is replaced by the optic nerve. The optic axes make an angle of 72° with each other at 40 mm.	

Stages of Foetal Development

Age of foetus	Condition of eye	General body form
During the 3rd month	The third period of retinal development begins. Growth of the margin of the optic cup forward to form the epithelium of the ciliary body and iris is commencing. Vessels appear in the optic nerve and a vein accompanies the hyaloid artery as far as the disc. The vasa hyaloidea propria atrophy. The arteria centralis retinae begins to branch on the disc. The outer layer of the choroid appears. Descemet's and Bowman's membranes form. The suspensory ligament of the lens begins to form. The ciliary muscle appears. The sclerotic condensation is visible all round the eye. The eyelids come together and adhere.	During the 3rd month the embryo becomes a foetus. The head grows less rapidly, though it is still large in proportion. The neck increases in length. Nails begin to appear on the fingers and toes. The arms are longer than the legs. The skin is red. The proctodaeum is formed and the external genitalia differentiated. The umbilical loop of gut is withdrawn into the abdomen in the middle of the month.
During the 4th month	The sphincter pupillae begins to differentiate from the margin of the ectodermal iris. The tunica vasculosa lentis begins to retrogress, especially its posterior and lateral portions. The ciliary body is formed and the middle layer of the choroid appears. Elastic fibres become visible in the cornea. The	Hairs develop on the skin and the disproportion between the fore and hind limbs disappears. They are both the same length.

Digitized by Illinois College of Optometry Library

Age of foetus	Condition of eye	General body form
	puncta lacrimalia become patent. Short eyelashes are present.	
During the 5th month	The layers of the choroid are complete and the outer layer contains chromatophores. Four superimposed sets of vessels are visible in the mesodermal iris. The meridional portion of the ciliary muscle is complete. The increased curve of the cornea is now apparent.	Sebaceous matter begins to be secreted by the skin. The legs become longer than the arms.
During the 6th month	The circular fibres of the ciliary muscle are formed. The lids begin to reopen. Eyelashes and eyebrows are better developed.	The skin becomes wrinkled and the hair longer.
During the 7th month	The pars plana of the ciliary epithelium is present though narrow. The main trunk of the hyaloid artery shrinks considerably, and the pupillary membrane also begins to atrophy in its central part. Medullation begins at the central end of the optic nerve.	Deposit of sub-cutaneous fat begins, so that the skin is no longer wrinkled.
During the 8th month	The macula begins to shew definite differentiation (third period of macular development). The retinal layers are fully developed elsewhere.	The skin is completely covered with sebum, and is paler in colour. The umbilicus is further from the pubis, but not yet in the centre of the body.
During the 9th month	The pupillary membrane and the hyaloid artery have practically disappeared. The medullation of the optic nerve reaches the lamina cribrosa at birth.	The hair on the body begins to disappear but that on the head grows longer. The foetus is much plumper and the umbilicus is in the centre of the body.

Digitized by Illinois College of Optometry Library

BIBLIOGRAPHY

I. Works of Historical Interest Published between 1750 and 1850

1751. Albinus. Adnotationes Academicae. L. I, c. 8.
1755. Zinn. Descrip. Anat. oc. hum. Göttingen.
1762. Hunter. Medical Commentaries. London. Vol. I.
1772. Wrisberg. Novi com. Soc. reg. Göttingen, T. II, et Opuscula anat. T. I.
1803. Heldius. De membrana pupillari. Gryph.
1814. Edwards. Meckel's Archiv. Bd I.
1818. Cloquet. Mémoire sur la membrane pupillaire et sur la formation du petit cercle art. de l'iris. Paris.
1819. Baerens. Diss. sist. Systematis lentis crystallinae monographia. Tübingen.
1832. Arnold. Anatomische und physiologische Untersuchungen über das Auge des Menschen.
1832. Henle. De membrana pupillari aliisque oculi membranis pellucentibus observationes anatomicae. Dissertatio inauguralis.
1833. Reich. De membrana pupillaris. Diss. Anat. Berlin.
1833. Valentin. Zur Anatomie des Foetus Auges der Säugethiere. Zeitschr. f. die Ophthalmologie.
1847. Brücke. Anatomische Beschreibung des menschlichen Augapfels.
1848. Schöler. De oculi evolutione in embryonibus gallinaceis. Diss. inaug. Dorpat.

II. Publications after 1850, Arranged in Order of Date and Grouped as far as Possible

A. *General (including comparative development, malformations and experimental embryology)*

1858. von Ammon, A. Die Entwicklungsgeschichte des menschlichen Auges. Archiv f. Ophth. Prof. Arlt, Donders u. Graefe. Berlin.
1863. Babuchin. Beiträge zur Entwicklung des Auges. Würzburger naturwissenschaftlicher Zeitschr. Bd IV.
1866. Schweigger-Seidel. Anatomische Mittheilungen. Virchow's Archiv. Bd XXXVII.
1872. Leiberkuhn, N. Über das Auge des Wirbelthierembryo. Schriften der Gesellschaft zur Beförderung der gesammten Naturwissenschaften zu Marburg. Bd X.
1874. Arnold. Beiträge zur Entwicklungsgeschichte des Auges.
1874. Schwalbe, G. Graefe-Saemisch Handbuch der gesammten Augenheilkunde. Bd I.
1875. Manz, W. Die Missbildungen des menschlichen Auges. Graefe-Saemisch Handbuch der gesammten Augenheilkunde. Bd II.
1875. Müller, W. Beiträge zur Anat. u. Physiol. Bd II.
1877. Bergmeister. Beiträge zur Entwicklungsgeschichte des Säugethierauges. Mittheilgs d. embryolog. Inst. der k. k. Univ. in Wien. Bd VI.
1877. Kessler. Zur Entwicklung des Auges der Wirbelthiere. Leipzig.
1877. Lieberkühn. Zur Anatomie des embryonalen Auges. Marburg. Sitzungsber. Bd VIII.

Digitized by Illinois College of Optometry Library

1877. Müller, W. Über die Stammesentwicklung des Sehorgans der Wirbelthiere. Centralblatt f. die med. Wissensch. Bd xv, S. 372.
1882. Kölliker. Embryologie de l'homme et des animaux supérieurs.
1883. Schwalbe, G. Lehrbuch der Anatomie des Auges. 1st ed. 1883. 2nd ed. 1887.
1884. Königstein, L. Histologische Notizen. Arch. f. Ophth. Bd xxx.
1886. Henle. Handbuch der systematische Anatomie. Braunschweig.
1890. His, W. Histogenese und Zusammenhang der Nervenelemente. Archiv f. Anat. u. Physiol. Anat. Abth. Suppl. p. 108.
1891. Cirincione, G. Sui primi stadi dell' occhio umano. Giornale dell' associazione Napolitana dei medici e naturalisti. Anno II, puntata 4 *a*.
1892. Merkel, Fr. u. Orr, A. Das Auge des Neugeborenen an einem schematischen Druckschnitt erläutert. Anat. Hefte. Bd I, Heft 3, S. 271.
1892. Minot, C. S. Human embryology. New York.
1893. Herr, F. Beitrag zur Entwicklungsgeschichte des menschlichen Auges. Med. Diss. Berlin.
1895. Keibel, F. Studien zur Entwicklungsgeschichte des Schweines. Schwalbe's Morphol. Arbeit. Bd v, S. 17.
1895. Weiss. Das Wachstum des Auges. Extra suppl. of Klin. Monatsblat. f. Augenheilk. Bd xxxiii, S. 218.
1896. Dieckmann. Beiträge zur Anatomie und Physiologie des neugeborenen Auges. Inaug. Diss. Marburg.
1897. Hoffmann, C. Beiträge zur Entwicklungsgeschichte der Selachii. Morph. Jahrb. Heft 1, Bd xxiv, 1896, und Heft 2, Bd xxv, 1897.
1897. Keibel, F. Normentafel zur Entwicklung des Schweines. Jena.
1898. Henckel, Fr. Beiträge zur Entwicklungsgeschichte des menschlichen Auges. Anat. Hefte. Bd x, Heft 33, S. 485 (also as Med. Diss. Giessen. 1898).
1898. Hippel, E. von. Über das normale Auge des Neugeborenen. Graefe's Archiv f. Ophthal. Bd xlv, S. 186.
1898. Hippel, E. von. Das Auge des Neugeborenen. Bericht über die 26 Vers. der ophthalm. Gesellsch. Heidelberg.
1898. Kollmann, J. Lehrbuch der Entwicklungsgeschichte des Menschen. Jena.
1898. Strahl, H. Zur Entwicklungsgeschichte des menschlichen Auges. Anat. Anz. Bd xiv.
1898. Tornatola, S. Ricerche embriologiche sull' occhio dei vertebrati. Atti della R. Accad. Peloritana. Vol. xiii.
1900. Halben, R. In welchem Verhältniss wächst das menschlichen Auge von der Geburt bis zur Pubität. Med. Diss. Breslau.
1900. Hippel, E. von. Die Missbildungen und die angeborenen Fehler des Auges. Graefe-Saemisch Handbuch der gesammten Augenheilkunde. 2nd ed. Bd II, 1, 1908. Published first in 1900.
1900. Virchow, H. Ergebnisse der Anatomie und Entwicklungsgeschichte. Merkel und Bonnet. Bd x.
1901. Spemann, H. Über Correlationen in der Entwicklung des Auges. Verh. anat. Gesellsch. 15 Vers. Bonn. Anat. Anzeig. Bd xix. Suppl. p. 61.
1901. Zumstein und Osaki. Bericht über die 29 Vers. d. Oph. Gesell. Heidelberg.
1901. Zumstein. Modelle zur Entwicklung des Auges. Marburg. Sitzber. S. 54.
1902. Baratz, W. Das Wachstum des Auges und seine Besonderheiten beim Neugeborenen. Inaug. Diss. St Petersburg. Bd ix. (Abstract in Schwalbe's Jahresbericht. New series. III, p. 864.)

Digitized by Illinois College of Optometry Library

1902. Brachet, A. Recherches sur l'ontogenèse des Amphibiens urodèles et anures. Arch. de Biol. T. xix.
1903. Collins, T. and Parsons, J. H. Anophthalmos and microphthalmos in a chick. Trans. Ophth. Soc. U.K. Vol. xxiii, p. 241.
1903. Hippel, E. von. Embryologische Untersuchungen über die Entstehungsweise der typischen angeborenen Spaltbildungen (Kolobome) des Augapfels. Arch. f. Ophth. Bd lv, S. 507.
1903. Graham Kerr. The development of Lepidosiren paradoxa. Quart. Journ. Micros. Sci. Pt III, vol. xlvi, p. 417.
1904. Boveri, Th. Über die phylogenetische Bedeutung der Sehorgane des Amphioxus. Zool. Jahrb. Suppl. Bd vii. (Festschr. f. Weismann.)
1904. Druault, A. Appareil de la vision. Traité d'anatomie humaine. Poirier et Charpy. T. v, p. 1018.
1904. van Duyse. Éléments d'embryologie et tératologie de l'œil. Paris.
1904. Lewis, W. H. Experimental studies on the development of the eye in Amphibia. Amer. Journ. of Anat. Vol. iii.
1905. Froriep, A. Die Entwicklung des Auges der Wirbelthiere. Hertwig's Handbuch. Bd ii, 2, S. 244.
1905. Froriep, A. Über die Einstülpung der Augenblase. Arch. f. mikr. Anat. Bd lxvi.
1906. Froriep, A. Über die Herleitung des Wirbelthierauges vom Auge der Ascidienlarve. Verh. Anat. Gesellsch. (Rostock, 1906.) Anat. Anz. Suppl. Bd xxix.
1906. Keibel, Fr. Die Entwicklungeschichte des Wirbeltierauges. Klin. Monatsbl. f. Augenheilk. Bd xliv. New series. Bd ii, S. 112.
1906. Keibel, F. Die äussere Körperform und der Entwicklungsgrad der Organe bei Affenembryonen. 9th part of Selenka's Menschenaffen. Wiesbaden.
1906. Keil, R. Beiträge zur Entwicklungsgeschichte des Auges vom Schwein, mit besonderer Berücksichtigung des Verhaltens der foetalen Augenspalte. Anat. Hefte. Bd xxxii, Heft 96.
1906. Lewis, W. H. Experiments on the regeneration and differentiation of the central nervous system in Amphibian embryos. Amer. Journ. Anat. Vol. v, p. 9.
1906. Spemann, H. Über eine neue Methode der embryonalen Transplantation. Verh. Deutsch. Zool. Gesellsch. 18. Vers. Marburg S. 195.
1907. Brachet, A. Sur la signification morphologique de l'œil des vertébrés. Bull. Soc. Sci. méd. et nat. de Bruxelles.
1907. Buchanan, L. Notes on the comparative anatomy of the eye. Trans. Ophth. Soc. Vol. xxvii, p. 262.
1907. Szily, A. von. Ein nach unten und innen gerichtetes, nicht mit der Fetalspalte zusammenhängendes Kolobom der beiden Augenbecher, bei einem etwa vier Wochen alten menschlichen Embryo. Klin. Monatsbl. für Augenheilk. Bd xlv. Suppl. p. 201.
1908. Bryce, T. H. Embryology. Quain's Anatomy. 11th ed. Vol. i.
1908. Elze, C. Beschreibung eines menschlichen Embryo von ca. 7 mm. gr. L. Anat. Hefte. Bd xxxv, Heft 106.
1908. Fleischer. Beitrag zur pathologischen Anatomie und Pathogenese des Mikrophthalmus und Koloboms. Graefe's Archiv f. Ophth. Bd lxviii, S. 427.
1908. Hochstetter, F. Bilder der äusseren Körperform einiger menschlicher Embryonen. München.

Digitized by Illinois College of Optometry Library

1908. Keibel und Elze. Normentafel zur Entwicklungsgeschichte des Menschen. Jena.
1908. Lange, O. Einblicke in die embryonale Anatomie und Entwicklung des Menschenauges. Nach einigen Präparaten dargestellt. Wiesbaden.
1908. Low, A. Description of a human embryo of 13–14 mesodermic somites. Journ. of Anat. and Physiol. Vol. xlii. Third ser. Vol. iii.
1908. Nussbaum, M. Entwicklungsgeschichte des menschlichen Auges. Graefe-Saemisch Handbuch der gesammten Augenheilkunde. Heft i, Bd ii.
1908. Spemann, H. Neue Versuche zur Entwicklung des Wirbelthierauges. Verh. d. deutsch. Zool. Gesell. Stuttgart.
1909. Coats. Ophthalmoscope. Vol. i, p. 724.
1909. Lubosch, W. Besprechung einer neuen Theorie der Licht- und Farbenempfindung nebst einem Exkurs über die stammesgeschichtliche Entstehung des Wirbelthierauges. Morph. Jahrb. Bd xxxix, S. 146.
1909. Merkel, F. Betrachtungen über die Entwicklung des Bindegewebes. Mit 39 Abbildungen aus den Tafeln. Anat. Hefte.
1909. Stockard, C. R. The development of artificially produced cyclopean fish. Journ. Exp. Zool. Vol. vi.
1911. Druault, A. Développement de l'organe de la vision et anatomie du globe de l'œil. Traité d'anatomie humaine. Poirier et Charpy. T. v.
1911. Szily, A. von. Über die entwicklungsgeschichtlichen Grundlagen für die Erklärung der kongenitalen Defektbildungen am Auge. Ber. über d. 37 Vers. d. ophth. Gesellsch. Heidelberg. Bergmann. Wiesbaden.
1911. Szily, A. von. Über die Entwicklung des melanot. Pigmentes im Auge der Wirbelthierembryonen und in Choroidealsarcomen. Archiv f. mikros. Anat. Bd vii.
1911, 1912 and 1914. Bach, L. and Seefelder, R. Atlas zur Entwicklungsgeschichte des menschlichen Auges. Pts 1, 2 and 3. Leipzig.
1912. Keibel and Mall. Manual of human embryology. Vol. ii, p. 218.
1912. Nussbaum, M. Entwicklungsgeschichte des menschlichen Auges. 3 Auflage. Leipzig. S. 104.
1912. Spemann, H. Zur Entwicklung des Wirbelthierauges. Zool. Jahrb. Abt. f. allg. Zool. u. Physiol. Bd xxxii.
1912. Szily, A. von. Über die primären Ursachen der Missbildungen des Auges. Ber. über d. 38. Vers. d. ophth. Gesellsch. Heidelberg.
1913. Franz. Lehrbuch der vergleichenden mikroskopischen Anatomie der Wirbelthiere. A. Oppel. 7e Teil. Sehorgan. Jena.
1913. Stockard, C. An experimental study of the optic Anlage in Amblyostoma punctatum with a discussion of certain eye defects. Amer. Journ. Anat. Vol. xv.
1914. Brachet, A. Recherches sur l'embryologie des reptiles. Arch. de Biol. T. xxix.
1914. Stockard, C. The artificial production of structural arrests and racial degeneration. Proc. New York Path. Soc. N.S. Vol. xiii.
1918. Guyer, M. F. and Smith, E. Studies in Cytolysins. 1. Some prenatal effects of lens antibodies. Journ. of Exp. Zool. Vol. xxv.
1920. Guyer and Smith. Studies in Cytolysins. 2. Transmission of induced eye defects. Journ. of Exp. Zool. Vol. xxvii.
1920. Szily, A. von. Das Problème der Augenbecherspalte, seine Beziehung zur normalen Entwicklung und zu den Missbildungen der Papilla nervi optici. Ber. über d. 42 Vers. d. dtsch. ophth. Gesellsch. Heidelberg. Bergmann. Wiesbaden.
1921. Koyanagi. Embryologische Untersuchungen über die Genese der

Digitized by Illinois College of Optometry Library

Augenkolobome und des Mikrophthalmus mit Orbitalcyste. Graefe's Archiv f. Ophth. Bd CIV.

1921. VOGT, A. Atlas de microscopie de l'œil vivant éclairé au moyen de la lampe à fente de Gullstrand. Berlin. 1921.

1922. COLE, W. H. The transplantation of skin in frog tadpoles with special reference to the adjustment of grafts over eyes and to local specificity of integument. Journ. Exp. Zool. Vol. XXXV, No. 4.

1922. GUYER, M. F. The production and transmission of certain eye defects. Trans. of Intern. Congress of Ophthal. Washington, D.C.

1922. KOYANAGI. Seltener Netzhautbefund bei einem Mikrophthalmus mit Orbitalcyste, nebst Bemerkungen über die formale Genese der Augenmissbildungen. Klin. Monatsbl. f. Augenheilk. Bd LXIX, S. 445.

1922. LINDAHL, C. and JOKL, A. Über den Verschluss der fötalen Augenbecherspalte, die Entwicklung der Sehnervinsertion und die Anlage des Pecten bei Vögeln. Zeitschr. f. d. ges. Anat. 1 Abt. München u. Berlin. Bd LXIII, S. 227.

1923. DEJEAN, C. Rôle du feuillet moyen dans l'assemblage des premières ébauches de l'œil. C.R. Acad. des Sci. 16 juillet.

1923. MCMURRICH. The development of the human body, a manual of human embryology. 7th ed. Philadelphia.

1923. MANN, I. C. Some suggestions on the embryology of congenital crescents. Brit. Journ. Ophth. August.

1924. KOLMER, W. Über das Auge des Eisvogels (Alcedo attis attis). Arch. f. d. ges. Physiol. Berlin. Bd CCIV, S. 266.

1924. KOLMER, W. Über die Augen der Fledermäuse. Zeitschr. f. d. ges. Anat. 1 Abt. München u. Berlin. Bd LXXIII, S. 644.

1924. MANN, I. C. Coloboma iridis and its embryology. Trans. Ophth. Soc. Vol. XLIV.

1924. SZILY, A. VON. Die Ontogenese der idiotypischen (erbbildlichen) Spaltbildungen des Auges, des Mikrophthalmos und der Orbitalcysten. Zeitschr. f. Anat. u. Entw. (1 Abt. d. Zeitschr. f. d. ges. Anat.) Bd LXXIV, Hefte 1/3.

1925. BRYCE, T. H. Measurements of very early human embryos. Zeits. f. d. ges. Anat. 1 Abt. München u. Berlin. Bd LXXVII, S. 493.

1925. LESER, O. Développement de la forme de l'œil humain. Arch. d'Opht. T. XLII, p. 81.

1925. POYNTER, C. W. M. and ALLEN, E. V. Lens antigen as a factor in congenital and hereditary eye anomalies. Amer. Journ. Ophth. Chicago. 3rd series, VIII, p. 184.

B. *The lens*

1872. BABUCHIN. Die Linse. Stricker's Handbuch der Lehre von den Geweben.

1874. ARNOLD. Die Linse und Strahlenplättchen. Graefe-Saemisch Handbuch der Augenheilkunde. Bd I.

1894. CIRINCIONE, G. Embriologia dell' occhio dei vertebrati. 1. Sullo sviluppo della capsula perilenticularis.

1895. DUCLOS, J. Étude sur les dimensions du crystallin. Thesis. Bordeaux.

1897. CIRINCIONE, G. Über die Entwicklung der capsula perilenticularis. Arch. f. Anat. u. Ent. Suppl.

1900. FISCHEL, A. Über die Regeneration der Linse. Anat. Hefte. Bd XIV.

1900. RABL, C. Über den Bau u. die Entwicklung der Linse. 1. Selachier und Amphibien. Zeitschr. f. wiss. Zool. Bd LXIII. 1898. 2. Reptilien und Vögeln. Bd LXV. 1899. 3. Säugethiere. Bd LXVII. 1900.

Digitized by Illinois College of Optometry Library

1903. Spemann, A. Über Linsenbildung bei defekter Augenblase. Anat. Anz. Bd xxiii.
1904. Lewis, W. H. Experimental studies on the development of the eye in Amphibia. I. On the origin of the lens. Amer. Journ. Anat. Vol. iii, p. 505.
1907. Spemann, H. Neue Tatsachen zum Linsenprobleme. Zool. Anz. Bd xxxi.
1910. Stockard, C. The independent origin and development of the crystalline lens. Amer. Journ. Anat. Vol. x.
1916. Fischel, A. Weitere Mitteilungen über die Regeneration der Linse. Arch. f. Entw.-Mech., Bd xv, 1902; and Über ruckläufige Entwicklung, ibid. xlii, 1916.
1920. Leplat, G. Note sur l'étude du développement du crystallin et des autres placodes chez les embryons monstrueux de Rana fusca. Extr. des Bull. de la classe des Sciences, 4 mai, p. 252.
1921. Mann, I. C. Congenital absence of the lens with special reference to an aphakic human embryo. Brit. Journ. Ophth. July.
1922. Mann, I. C. Absence of the lens occurring in the human embryo. Journ. of Anat. Vol. lvi. January.

C. *The retina, ciliary body, iridic epithelium and iris muscles*

1864. Ritter, C. Zur histologischen Entwicklungsgeschichte des Auges. Arch. f. Ophth. Bd x, Abt. 1, S. 60. Zweiter Beitrag zur Histogenese des Auges. Ibid. Bd x, Abt. 2, S. 142.
1867. Schultze, M. Bemerkungen über Bau und Entwicklung der Retina. Arch. f. mikros. Anat. Bonn. Bd iii, S. 215.
1876. Faber, C. Der Bau der Iris des Menschen u. der Wirbelthiere. Leipzig.
1877. Loewe, L. Histogenese der Retina. Centralblat. f. med. Wissensch. Berlin. Bd xv, S. 930.
1878. Loewe, L. Die Histogenese der Retina nebst vergleichenden Bemerkungen über die Histogenese des Centralnervensystems. Arch. f. mikros. Anat. Bonn. Bd xv, S. 596.
1880. Albertoni. Sul rosso della retina nel feto e nel neonato. Lo sperimentale. Firenze. Vol. xlv, p. 588.
1881. Angelucci. Über Entwicklung und Bau des vorderen Uvealtractus der Vertebraten. Arch. f. mikr. Anat. Bd xix.
1883. Vossius. Beiträge zur Anatomie des Nervus opticus. Archiv f. Ophth. Bd xxix, Heft 4, S. 119.
1885. Fuchs, E. Beiträge zur normalen Anatomie des menschlichen Iris. Graefe's Archiv f. Ophth. Berlin. Bd xxxi, Abt. 3.
1887. Chievitz, J. H. Die Area und Fovea centrales retinae beim menschlichen Fetus. Intern. Zeitschr. f. Anat. u. Physiol. Bd iv, S. 201.
1888. Chievitz, J. H. Entwicklung der fovea centralis retinae. Anat. Anzeig. Jena. Bd iii, S. 579.
1888. Falchi, F. Sur l'histogenèse de la rétine et du nerf optique. Arch. Ital. de Biol. Vol. ix, p. 382.
1888. Falchi, F. Über die Histogenese der Retina und des Nervus opticus. Graefe's Archiv f. Ophth. Bd xxxiv, Abt. 2, S. 67.
1889. Keibel, F. Über die Entwicklung des Sehnervens. Deutsch. Med. Wochenschr. Bd xv.
1891. Froriep, A. Über die Entwicklung des Sehnervens. Anat. Anzeig. Bd vi.

Digitized by Illinois College of Optometry Library

1891. Ucke, A. Zur Entwicklung des Pigmentepithels der Retina. St Petersburg.
1894. Juler, H. A contribution to the anatomy and physiology of the iris. Trans. 8th Internat. Opt. Cong., p. 67.
1895. Schön, W. Der Übergangsraum der Netzhaut oder die sogenannte Ora serrata. Archiv f. Anat. u. Entwicklungsgesch. S. 417.
1896. Held, R. Beitrag zur Kenntnis des Nervenmarks. 3. Über experimentale Reifung des Nervenmarks. Arch. f. Anat. und Physiol. Anat. Abth. S. 222.
1896. Ramón y Cajal, S. Nouvelles contributions à l'étude histologique de la rétine, etc. Journ. de l'Anat. et de la Physiol. Vol. xxxii.
1898. Grynfeltt, E. Le muscle de la pupille chez les mammifères. Thesis for Doctorate in Medicine. Montpellier.
1898. Grynfeltt, E. Sur le développement du muscle dilatateur de la pupille chez le lapin. Compt. Rend. Acad. Sci. Paris. Vol. cxxvii, p. 966.
1900. Heerfordt, C. Studien über den musculus dilatator pupillae, samt Angabe von gemeinschaftlichen Kennzeichen einiger Fälle epithelialer Muskulatur. Anat. Hefte. Bd xiv, Heft 46, S. 487.
1900. Heerfordt, C. Berichtigung zum Aufsatze über den musculus dilatator pupillae, etc. Anat. Hefte. Bd xv, Heft 49, S. 721.
1901. Lange, O. Zur Anatomie des Auges des Neugeborenen. 2. Suprachoroidealraum, zonula Zinii, ora serrata und sogenannte physiologische Exkavation der Sehnervenpapilla. Klin. Monatsbl. f. Augenheilk. S. 202.
1902. Herzog, H. Über die Entwicklung der Binnenmuskulatur des Auges. Arch. f. mikros. Anat. Bd lx, S. 517.
1902. Schultze, O. Überdie Entwicklung und Bedeutung der ora serrata des menschlichen Auges. Verh. Phys.-Med. Gesell. Würzburg. New series. Vol. xxxiv.
1902. Szily, A. von. Zur Anatomie und Entwicklungsgeschichte der hinteren Irisschichten, mit besonderer Berücksichtigung des musculus sphincter iridis beim Menschen. Anat. Anz. Bd xx, S. 161.
1902. Szily, A. von. Beitrag zur Kenntnis der Anatomie und Entwicklungsgeschichte der hinteren Irisschichten, mit besonderer Rücksichtigung des musculus sphincter pupillae des Menschen. Arch. f. Ophth. Bd liii.
1903. Bernard. Studies in the retina. Parts 3, 4 and 5. Journ. Micro. Soc. Vol. xliv, p. 25.
1904. Tornatola. Sulla membrana limitante interna della retina nei vertebrati. Nota prelim. Anat. Anz. Vol. xxiv.
1905. Forsmark. Zur Kenntnis des Irismuskulatur des Menschen, ihr Bau und ihre Entwicklung. Mitth. aus der Augenklinik des Carolin. Medico-Chirurgischen Institut zu Stockholm.
1905. Jacobi, E. Über die Neuroglia des Sehnerven. Klin. Monatsbl. f. Augenheilk. Bd xliii, S. 429.
1905. Tornatola, S. Sulla assenza della limitante interna nella retina dei Vertebrati. Atti della R. Accademia Peloritana. Vol. xx, fasc. 1. Messina.
1906. Krueckmann, E. Über die Entwicklung und Ausbildung der Stützsubstanz im Sehnerven und in der Netzhaut. Klin. Monatsbl. für Augenheilk. Bd xliv. New series. Vol. i, p. 162.
1908. Juselius. Die Entwicklung des hinteren Pigmentepithels des Iris aus der secundären Augenblase und sein Verhältniss zu der Iris musculatur und spontanen Iriscysten. Klin. Monatsbl. f. Augenheilk. Bd xlvi.

Digitized by Illinois College of Optometry Library

1908. Lauber. Beiträge zur Entwicklungsgeschichte und Anatomie der Iris. Arch. f. Ophth. Bd LXIII, S. 1.
1910. Magitot, A. Étude sur le développement de la rétine humaine. Ann. d'oculistique. T. CXLIII, p. 241.
1911. Seefelder, R. Nochmals zur Frage der Netzhautanomalien in sonst normalen fetalen menschlichen Augen. Archiv f. Ophth. Bd LXXIX.
1912. Szily, A. von. Über die einleitenden Vorgänge bei der ersten Entstehung der Nervenfasern im Nervus opticus. Graefe's Archiv f. Ophth. Bd LXXXI, Heft 1.
1913. Seefelder, R. Beiträge zur Entwicklung des menschlichen Auges mit besonderer Berücksichtigung des Verschlusses der fötalen Augenspalte. Anat. Hefte. Bd XLVIII, Heft 146. Bergmann. Wiesbaden.
1914. Speciale-Cirincione. Sullo sviluppo dei muscoli e degli strati posteriori dell' iride nell' uomo.
1921. Leplat, G. De la musculature interne de l'œil de quelques reptiles. Sur le développement de la musculature interne de l'œil des reptiles. Extr. des Bulletins de la classe des Sciences, 3 déc. p. 741.
1921. Mann, I. C. On the development of the fissural and associated regions in the eye of the chick with some observations on the mammal. Journ. of Anat. Vol. LV.
1921. Szily, A. von. Die Deutung der Zusammenhänge der wichtigsten Entwicklungsphasen des Wirbeltierauges. 1. Das Probleme der Becherspalte und die Entstehung der "papilla nervi optici primitiva seu epithelialis," u.s.w. A. Morphogenese an der Hand von Plattenmodellen nach Untersuchungen beim Kaninchen als Beispiel für den Typus "Säuger." Graefe's Archiv f. Ophth. Bd CVI, S. 195.
1922. Cattaneo. La struttura della retina nei vertebrati. Annali di Ottalm. e clin. oculist.
1922. Leplat, G. Recherches sur le développement du cône papillaire de l'œil des reptiles. Comptes rend. de l'association des Anatomistes. Avril.
1922. Mann, I. C. On the morphology of certain developmental structures associated with the upper end of the choroidal fissure. Brit. Journ. Ophth. April.
1922. Speciale-Cirincione. Sullo sviluppo dei muscoli e degli strati posteriori dell' iride. Annali di Ottalm. e clin. oculistica. Gennaio.
1922. Szily, A. von. Vergleichende Entwicklungsgeschichte der Papilla nervi optici und der sogenannten axialen Gebilde. 1. Morphogenese des Sehnerveintrittes und des "Fächer" beim Hühnchen als Beispiel für den Typus "Vogel." Graefe's Archiv f. Ophth. Bd CVII, Hefte 2/3. 2. Morphogenese des Sehnerveintrittes, der "Leiste" (processus falciformis) bei der Bachforelle. Ein Beispiel für die primitivste Papillenform in der Wirbelthierreihe oder eines "Reinen Becherspalttypus" der Knochenfische. Graefe's Archiv f. Ophth. Bd CIX, S. 1.
1923. Seefelder, R. Über die Faltenbildungen der embryonaler Retina. Archiv f. Ophth. Bd CXI, S. 83.

D. *Vitreous and suspensory ligament of lens*

1874. Kessler. Über die Entwicklung des Glaskörpers. Dorpat med. Zeitschr.
1886. Keibel, F. Zur Entwicklung des Glaskörpers. Archiv f. Anat. u. Physiol.

Digitized by Illinois College of Optometry Library

1889. Hache. Sur l'hyaloïde et la zone de Zinn. C.R. de la Soc. de Biol.
1891. Stuart and Anderson. On a membrane lining the fossa patellaris of the corpus vitreum. Proc. Roy. Soc. Vol. xlix.
1894. Retzius, G. Über den Bau des Glaskörpers und der zonula Zinii in dem Auge des Menschen und einiger Thiere. Biol. Untersuch. N.S. Bd vi.
1895. Schön, W. Zonula und ora serrata. Anat. Anz. Bd x, S. 360.
1897. Tornatola, S. Origine et nature du corps vitré. Résumé of communication made to 12th International Congress of Med. Moscow. Rev. gén. d'opht. Vol. xvi, 5, p. 543.
1898. Campos. De la portion réfléchie de la membrane hyaloïde. Arch. d'opht. Déc.
1899. Carini, A. Osservazioni sull' origine del vitreo. Monitore Zool. Ital. Vol. x. Suppl. p. 33.
1900. Bourzew. Sur les méthodes de coloration de la membrane hyaloïdienne. Société d'ophtalm. de St Petersbourg. Séance 20 mai. Westnik ophtalm. No. 2.
1901. Addario, C. Sulla struttura del vitreo embrionale e di neonati: sulla matrice del vitreo e sull' origine della zonula. Annali di Ottalm. e lavori della clinica oculistica di Napoli. Vol. xxx.
1901. Stampani, G. Alcune ricerche sull' origine e la natura del vitreo. Monit. Zool. Ital. Anno 12, p. 145.
1902. Addario, C. Über die Matrix des Glaskörpers im menschlichen und tierischen Auge. Anat. Anz. Bd cxxi, S. 9.
1902. Lenhossek. Die Entwicklung des Glaskörpers. Vortr. gehalt. in der Kgl. Akad. der Wissensch. in Budapest.
1903. Cirincione, G. Sullo stato odierno della questione riguardante la genese del vitreo. Siena. 1903 and 1905.
1903. Cirincione, G. Über die Genese des Glaskörpers bei Wirbeltieren. Centralbl. prakt. Augenheilk. Bd xxvii, S. 161.
1903. Cirincione, G. Über die Genese des Glaskörpers bei Wirbeltieren. Verh. Anat. Gesellsch. 17 Vers. Anat. Anzeig. Bd xxiii. Suppl. p. 51.
1903. Haemers, A. Régénération du corps vitré. Arch. d'ophtalm. Vol. xxiii, p. 103.
1903. Kölliker. Die Entwicklung und Bedeutung des Glaskörpers. Zeitschr. f. wissensch. Zoologie. Bd lxxvi. Verh. Anat. Gesellsch. 17 Vers. Heidelberg.
1903. Lenhossek, M. Die Entwicklung des Glaskörpers. Leipzig.
1903. Van Pee, P. Recherches sur l'origine du corps vitré. Arch. de Biol. Vol. xix, p. 317.
1903. Rabl, C. Zur Frage nach der Entwicklung des Glaskörpers. Anat. Anz. Bd xxii.
1903. Tornatola, S. Sull' origine della vitrea. (xvi° Congresso dell' Assoc. Ottal. Ital. Firenze.) Annali di Ottalm. e lavori della clinica oculistica di Napoli. Vol. xxxi.
1903. Truc et Vialletou. Anatomie de la zone de Zinn. Encyclopédie franç. d'opht.
1904. Addario, C. La matrice ciliare delle fibrille del vitreo, loro disposizione, e anche loro rapporti colla neuroglia della retina visiva periferica nell' occhio umano adulto. Arch. d'Ottal. Vol. xii.
1904. Cirincione, G. Über dem gegenwärtigen Stand der Frage hinsichtlich der Genese des Glaskörpers. Arch. f. Augenheilk. Bd. l, S. 201.
1904. Szily, A. von. Zur Glaskörperfrage. Anat. Anz. Bd xxiv, S. 417.

Digitized by Illinois College of Optometry Library

1905. Duyse, van. Développement du corps vitré. Encyclopédie franç. d'opht. Vol. xi. Paris.
1905. Venneman. La membrane hyaloïde du corps vitré. Soc. belge d'opht. Novembre.
1906. Wolfrum, M. Zur Genese des Glaskörpers. Ber. 33 Vers. Ophth. Ges. Heidelberg.
1907. Wolfrum, M. Zur Entwicklung und normalen Struktur des Glaskörpers. Arch. f. Ophth. Bd xlv.
1908. Szily, A. von. Über das Entstehen eines fibrillären Stutzgewebes im Embryo und dessen Verhältnis zur Glaskörperfrage. Anat. Hefte. Bd xxxv, Heft 107.
1911. Calderaro, S. Contributo allo studio dell' anatomia del vitreo assile negli embrioni e feti umani.
1911. Lenhossek, von. Die Entwicklung und Bedeutung der Zonulafasern nach Untersuchungen am Hühnchen. Archiv f. mikros. Anat. Bd lxxvii.
1911. Lenhossek, von. Die Entwicklung und Bedeutung der Zonula ciliaris. Verhandl. Anat. Ges. Erg. Heft. Anat. Anzeig. Bd xxxviii, S. 81.
1912. Franz. Histogenetische Theorie des Glaskörpers. Arch. f. Vergl. Ophth. 30 Juli.
1912. Mawas et Magitot. Étude sur le développement du corps vitré et de la zonule de Zinn chez l'homme. Arch. d'anat. micros. T. xiv.
1913. Druault, A. Sur le développement du corps vitré de la zonule. Bibliogr. anatomique. Fasc. 1, t. xxiii.
1913. Leboucq. La névroglie rétino-vitréenne. Compt. rend. de la Soc. Belge de Biol. T. xcix.
1914. Druault, A. and S. Recherches sur les derniers stades du développement du corps vitré et de l'appareil suspenseur du crystallin chez l'orvet. Actes du xii Congrès intern. d'opht. St Petersbourg.
1914. Druault, A. Développement de l'appareil suspenseur du crystallin chez l'homme et la souris. Arch. d'opht. Bd xxxiv, p. 1.
1921. Monesi. Contributo allo studio della genese del vitreo nei vertebrati. Atti della Soc. Lombarda di scienze mediche e biolog. Vol. x, No. 2. Febbraio.
1922. Beauvieux. La zonule (étude topographique et histologique). Arch. d'opht. Vol. xxxix. Juillet et août.
1923. Dejean, Ch. Origine du corps vitré et de la zonule. C.R. Acad. des Sciences. 30 Juillet.
1923. Fracassi, G. Entwicklung und Morphologie des Glaskörpers beim Menschen und bei einigen Säugetieren. Archiv f. Ophth. Bd cxi, S. 219.
1924. Fracassi, G. Bemerkungen zur Embryologie des Auges. Arch. f. Ophth. Bd cxv, S. 215.
1924. Dejean, Ch. Sur la formation des milieux figurés de l'œil des vertébrés. Arch. d'opht. Par. xli, p. 659.
1924. Dejean, Ch. Origine collagène du corps vitré et de la zonule de Zinn dans l'œil des vertébrés. Thèse pour le Doctorat ès sciences naturelles. Paris. Arch. d'Anat. micro. Par. xxi, p. 3.
1925. Carrère, L. De l'origine ciliaire des fibres de la zonule. Compt. rend. de la Soc. de Biol. Vol. xciii, p. 769.
1926. Dejean, Ch. Sur l'origine des fibres de la zonule. Compt. rend. de la Soc. de Biol. Vol. xcii, 4 juin.
1926. Dejean, Ch. Étude anatomique et embryologique sur la membrane hyaloïde de l'œil des mammifères. Son rôle dans la formation des milieux de l'œil, ses limites, sa structure. Arch. d'opht. Vol. xliii, No. 5. Mai. Paris.

Digitized by Illinois College of Optometry Library

E. *Associated mesoderm*

1. Blood system

1869. Richiardi, S. Sopra il sistema vascolare sanguifero dell' occhio del feto umano e dei mammiferi.

1881. Konigstein, L. Über die Pupillarmembran. Archiv f. Ophth. Bd xxvii, Abt. 3.

1892. Schultze, O. Zur Entwicklungsgeschichte des Gefässsystems im Säugetierauge. Kölliker's Festschrift. Leipzig.

1892. Voll, A. Über die Entwicklung der membrana vasculosa retinae. Kölliker's Festschrift, gewidmet vom anat. Instit. zu Würzburg.

1896. Deyl, J. Über den Eintritt der Art. cent. retin. beim Menschen. Anat. Anz. Bd xi, S. 687.

1900. Versari, R. Morfologia dei vasi sanguiferi arteriosi dell' occhio umano e di altri mammiferi. Ric. fatte nel laborat. di anatomia umana normale della R. Università di Roma ed in altri laborat. biologici. Vol. vii, fasc. 3 e 4.

1900. Versari, R. Contributo alla conoscenza della morfogenese degli strati vascolari della coroide nell' occhio dell' uomo e di altri mammiferi. Ric. fatte nel laborat. di anat. norm. della R. Università di Roma ed in altri laborat. biol. Vol. viii, p. 5. (Abstract in Arch. Ital. de Biol. Vol. xxxvi, p. 357.)

1901. Corrado, G. Circa l' osservazione della membrana capsulo-pupillare (tunica vasculosa lentis). Giornale dell' Assoc. Napol. dei medici e naturalisti. Vol. xi, p. 5.

1901. Virchow, H. Fächer, Zapfen, Leiste, Polster, Gefässe im Glaskörperraum von Wirbeltieren, sowie damit in Verbindung stehende Fragen. Ergebnisse Anat. und Entwickl. Bd x, S. 720.

1903. Versari, R. La morfogenese dei vasi sanguiferi della retina umana. Ricerche fatte nel laborat. di anat. umana, ecc. Vol. x, fasc. 1. (Abstr. in Arch. Ital. de Biol. Vol. xli, p. 482.)

1905. Fuchs, H. Entwicklungsgeschichte des Wirbeltierauges. 1. Über die Entwicklung der Augengefässe des Kaninchens. Anat. Hefte. Bd xxviii, Heft 84, S. 1.

1907. Breuckner, A. Über Persistenz von Resten der tunica vasculosa lentis. Arch. f. Augenheilk. Bd lvi. Suppl. p. 5.

1908. Dedekind, F. Beiträge zur Entwicklungsgeschichte der Augengefässe des Menschen. Bd xxxviii, Heft 114, S. 1.

1908. Leber, T. Die Zirkulations- und Ernährungsverhältnisse des Auges. Graefe-Saemisch Handbuch der ges. Augenheilk. 2nd ed. Bd xxii.

1909. Versari, R. Über die Entwicklung der Blutgefässe des menschlichen Auges. Anat. Anz. Bd xxxv, S. 105.

1909. Cosmettatos, G. F. Recherches sur le développement de la membrane pupillaire chez l'homme. Arch. d'opht. T. xxx, p. 480.

1913. Maggiore, L. Sul comportamento dei vasi sanguigni nel segmento anteriore della "tunica vasculosa oculi" degli uccelli. Ricerche fatte nel laboratorio della R. Università di Roma, ecc.

1919. Versari, R. La morphogenese dei rami collaterali e terminali delle arterie ciliare posteriori lunghe ed il comportamento, non ancora descritto, dei vasi sanguiferi reflui dalla membrana pupillare nell' occhio embrionale umana. Ricerche fatte nel laborat. di anatomia umana della R. Università di Roma. Vol. xix, fasc. 3 e 4.

Digitized by Illinois College of Optometry Library

1922. Wolfrum. Über den Bau der Irisvorderfläche des menschlichen Auges mit vergleichend. anatomischen Bemerkung. Archiv f. Ophth. Bd cix, S. 106.
1923. Versari, R. Le fasi di sviluppo e di regresso della tunica vasculosa lentis e la morfogenese dei vasi sanguiferi nei processi ciliari e nell' iride dell' uomo. Estratto da Ricerche di Morfologia. Vol. iii, fasc. 2 e 3.
1925. Mann, I. C. The development of the human iris. Brit. Journ. Ophth. October.

2. Ciliary muscle

1901. Lange, O. Zur Anatomie des Auges des Neugeborenen. 1. Zur Anatomie des Ciliarmuskels der Neugeborenen. Klin. Monatsbl. f. Augenheilk. Bd xxxix, S. 1.

3. Cornea, sclerotic and anterior chamber

1879. Gerlach. Über die Beziehung des ciliaren Ursprungs der Iris zu dem Brucke'schen Muskel. Sitzungb. der Phys.-med. Soc. zu Erlangen.
1895. Gabriélides, A. Recherches sur l'embryogénie et l'anatomie comparée de l'angle de la chambre antérieure chez le poulet et chez l'homme. Muscle dilatator de la pupille. Thesis, Paris; and in Arch. d'opht., t. xv, p. 176.
1896. Jeannulatos, P. Recherches embryologiques sur la mode de formation de la chambre antérieure chez les mammifères et chez l'homme. Embryogénie de la membrane pupillaire, part qu'elle prend dans l'évolution de l'iris. Thesis, Paris; and in Arch. d'opht., t. xvi, p. 529.
1906. Fritz, W. Über die Membrana Descemetii und das Ligamentum pectinatum iridis bei den Säugetieren und beim Menschen. Sitzber. K. K. Akad. Wiss. Wien. Math.-naturwiss. Kl. Bd cxv.
1906. Hirsch, K. Ist die foetale Hornhaut vascularisiert? Klin. Monatsb. f. Augenheilk. Bd xliv, Abt. 2, S. 13.
1906. Seefelder und Wolfrum. Zur Entwicklung der vorderen Kammer und des Kammerwinkels beim Menschen, nebst Bemerkungen über ihre Entstehung bei Tieren. Arch. f. Ophth. Bd lxiii, S. 430.
1909. Knape, V. Über die Entwicklung der Hornhaut des Hühnchens. Anat. Anz. Bd xxxiv, S. 417.
1913. Speciale-Cirincione. Sullo sviluppo della camera anteriore dell' occhio umano. Roma.
1923. Laguesse. Les lamelles primitives de la cornée du poulet sont comme le corps vitré d'origine mésostromale-ectodermique. C.R. Soc. de Biol. Vol. lxxxix, No. 25.

F. *The orbit and its contents*

1. Extrinsic muscles

1882. Van Wijhe, J. Über die Mesodermsegmente und die Entwicklung der Nerven der Selachierkopfes. Verh. Königl. Akad. Wiss. Amsterdam.
1882. Van Wijhe, J. Über das Visceralskelett und die Nerven des Kopfes der Ganoiden und von Ceratodus. Niederl. Arch. f. Zool. Bd v.
1890. Oppel, A. Über Vorderkopfsomiten und die Kopfhöhle von Anguis fragilis. Archiv f. mikros. Anat. Bd. xxxvi.
1891. Platt, J. A. A contribution to the morphology of the vertebrate head, based on a study of Acanthias vulgaris. Journ. of Morph. Vol. v.

Digitized by Illinois College of Optometry Library

1894. Weiss, L. Über das Verhalten des musculus rectus externus und internus bei wachsenden Divergenz der Orbita. Arch. f. Augenheilk. Bd xxix, S. 298.
1895. Sewertzoff, A. Die Entwicklung der Occipitalregion der niederen Vertebraten in Zusammenhang mit der Frage nach der Metamerie des Kopfes. Bull. Soc. Nat. Moscow.
1896. Nussbaum, M. Nerv und Muskel. 1. Mitteilung. Arch. f. mikros. Anat. Bd xxxvii, S. 416.
1897. Neal, H. The segmentation of the nervous system in Squalus acanthias. Bull. Mus. Comp. Zool. Harvard College. Vol. xxxi.
1897. Platt, I. A. The development of the cartilaginous skull and of the branchial and hypoglossal musculature in Necturus. Morphol. Jahrsber. Vol. xxv.
1897. Reuter, K. Über die Entwicklung der Augenmuskulatur beim Schwein. Anat. Hefte. Bd ix, S. 365.
1897. Rex, H. Über das Mesoderm des Vorderkopfes der Ente. Arch. f. mikros. Anat. Bd l.
1897. Weiss, L. Über das Wachstum der menschlichen Auges und über die Veränderung der Muskelinsertionen am wachsenden Auge. Anat. Hefte. Bd viii, Heft 25, S. 191.
1898. Neal, H. The problem of the human head. Journ. Comp. Neur. Vol. viii.
1898. Sewertzoff, A. Studien zur Entwicklung des Wirbeltierkopfes. 2. Die Metamerie des Kopfes des elektrischen Rochen. Bull. Soc. Nat. Moscow.
1898. Zimmermann, K. Über Kopfhöhlenrudimente beim Menschen. Arch. f. mikros. Anat. Bd liii, S. 481.
1899. Corning, H. Über die Entwicklung der Kopf- und Extremität-muskulatur. Morphol. Jahrb. Bd xxviii.
1899. Nussbaum, M. Entwicklung der Augenmuskeln bei den Wirbeltieren. Sitzber. Niederrhein. Ges. f. Natur- u. Heilk. Bonn.
1900. Corning, H. Über die verg. Anat. der Augenmuskulatur. Morph. Jahrb. Bd xxix.
1905. Johnston, J. B. The morphology of the vertebrate head from the viewpoint of the functional divisions of the nervous system. Journ. Comp. Neurol. u. Psychol. Vol. xv, p. 175.
1907. Brachet, A. Recherches sur l'ontogenèse de la tête chez les amphibiens. Arch. de Biol. T. xxiii.
1926. Kingsbury, B. F. Branchiomerism and the theory of head segmentation. J. Morph. Phil. 1926–7. Vol. xliii, p. 83.

2. The lids and lacrimal apparatus

1881. Legal, E. Zur Entwicklungsgeschichte des Tränennasenganges bei Säugetieren. Med. Diss. Breslau.
1883. Born, G. Die Nasenhöhlen und der Tränennasengang der amnioten Wirbeltiere. 1. Morph. Jahrbuch. Bd v, S. 62. 1879. 2. Ibid. Bd v, S. 401. 3. Ibid. Bd viii, S. 188.
1883. Legal, E. Die Nasenhöhlen und der Tränennasengang der amnioten Wirbeltiere. 4. Morph. Jahrbuch. Bd viii, S. 353.
1890. Seiler, H. Zur Entwicklung der Conjunktivalsackes. Arch. f. Anat. und Phys.
1894. Kirschstein, F. Über die Tränendrüse des Neugeborenen und die Untersuchung derselben von den Erwachsenen. Med. Diss. Berlin.

Digitized by Illinois College of Optometry Library

1898. Cosmettatos, G. F. Recherches sur le développement des voies lacrimales. Thesis. Paris.
1899. Axenfeld, T. Bemerkungen zur Physiologie und Histologie der Tränendrüse. Bericht über d. 27 Vers. der Ophth. Gesell. Wiesbaden.
1899. Dewecker, L. Das Weinen und die Tränen der Neugeborenen. Klin. Monatsbl. f. Augenheilk. Bd xxxviii, S. 220.
1904. Monesi, L. Die Morphologie der foetalen Tränenwege beim Menschen. Klin. Monatsbl. f. Augenheilk. Jahrg. 42. Bd i, S. 1.
1905. Falchi, F. Sur le développement de la glande lacrimale. Arch. Ital. de Biol. Vol. xliv, p. 412.
1906. Fleischer, B. Die Entwicklung der Tränenröhrchen bei den Säugetieren. Graefe's Archiv f. Ophth. Bd lxii, S. 279.
1906. Matys, V. Die Entwicklung der Tränenableitungswege. Zeitschr. f. Augenheilk. Bd xiv, S. 222. 1905. Heft 2. Ibid. Bd xvi, S. 303. 1906.
1907. Ask, F. Über die Entwicklung der caruncula lacrimalis beim Menschen nebst Bemerkungen über die Entwicklung der Tränenröhrchen und der Meibom'schen Drüsen. Anat. Anz. Bd xxx, S. 197.
1908. Ask, F. Über die Entwicklung der Lidränder, der Tränenkarunkel und der Nickhaut beim Menschen, nebst Bemerkungen zur Entwicklung der Tränenabführungswege. Anat. Hefte. Bd xxxvi, Heft 109.
1908. Contino. Über Bau und Entwicklung des Lidrandes beim Menschen. Graefe's Arch. f. Ophth. Bd lxvi.
1908. Goez. Untersuchung von Tränendrüsen aus verschiedenen Lebensaltern. Med. Diss. Tübingen.
1908. Speciale-Cirincione. Über die Entwicklung der Tränendrüse beim Menschen. Graefe's Archiv f. Ophth. Bd lxix.
1908. Speciale-Cirincione. Sullo sviluppo della ghiandola lacrimale nell'uomo. Naples. V. Pasquale.
1910. Ask, F. Studien über die Entwicklung des Drüsenapparates der Bindehaut beim Menschen. Anat. Hefte. Bd xl, Heft 122.
1911. Contino. Embryologie de la caroncule et du repli semilunaire chez l'homme. Arch. d'opht. Vol. xxxi.
1911. Lang, P. Zur Entwicklung der Tränenausführapparates beim Menschen. Anat. Anzeig. Bd. xxxviii, S. 561.
1911. Riquier, G. C. Contributo allo studio della ghiandola lacrimale umana. Monit. Zool. Ital. Vol. xxii, p. 56.

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

INDEX

Acanthias, 138, 253
Ali-sphenoid, 42, 265, 267
Amacrine cells, 80, 90, 97, 99, 103, 112, 270, 273
Amia calva, 98, 270
Amnion, 1, 2
Amniotic cavity, 2
Amphioxus, 10
Anencephaly, retina in, 148
Annular pad of lens, 270
Annular vessel, 36, 192, 197, 198
Anophthalmia, 28
Anterior cerebral plexus, 192
Anterior chamber, 38, 41, 239
  angle of, 41, 237, 243 *et seq.*; in adult, 242
Anterior lenticonus, 30
Anterior neural fold, 6
Anterior polar cataract, 30, 66
Anthropoid, 44
Aphakia, 29
Arc line (Bogenlinie), 175
Archenteric cavity, 2
Archenteron, 2
Arrectores pilorum, 34, 123
Artery, central, of retina, 37, 73, 197, 230 *et seq.*
  cilio-retinal, 233
  common ciliary, 196
  hyaloid, 22, 31, 36, 192, 203, 213, 230, 232
  internal carotid, 193, 195, 198
  long ciliary, 197
  nasal ciliary, 196
  ophthalmica interna, 194, 198
  posterior ciliary, 197, 233
  temporal long ciliary, 196
Ascidian larva, 7

Basi-sphenoid, 267
Bergmeister's papilla, 109
Binocular vision, 44
Bi-polar cells, 80, 93, 99, 101
Birds, 43, 269, 272
Blastomeres, 2
Blastula or blastocyst, 2
Body stalk, 2
Bowman's membrane, 238, 241
Bruch, membrane of, 199

Canal, of Cloquet, *see* Cloquet's canal
  of Schlemm, *see* Schlemm's canal
Capsula perilenticularis fibrosa, 164, 178, 204, 206
Capsulo-pupillary vessels, *see* Tunica vasculosa lentis, lateral portion
Carnivora, 43, 269
Caruncle, 260
Cauda of optic nerve, 269
Cavernous sinus, 192
Ceratodus Fosteri, 50
Cerebral vesicle, 276
Cheiroptera, 269
Chick embryo, 39, 158, 162, 272
Chievitz, transient fibre layer of, 80, 86, 89, 92, 98, 112, 270, 273
Choroid, 198 *et seq.*
  chorio-capillaris layer of, 200
  middle layer of, 202
  outer layer of, 200
Choroidal fissure, *see* Foetal fissure
Cilia, 81, 93 (*see also* Lashes)
Ciliary muscle, 39, 235
  circular fibres of, 247
Ciliary process, 33, 116 *et seq.*
  vessels of, 227 *et seq.*
Cloquet's canal, 173, 188
Collins, glands of, 119
Coloboma, of choroid, 39
  of iris, 34
  of retina, 29
Cones, 101
Congenital abnormalities, of associated mesoderm, 252
  of lens, 65
  of neural ectoderm, 145
  of optic vesicle, 27
  of vessels, 234
  of vitreous, 188
Congenitally cystic eye, 28
Conjunctiva, 15
Cornea, 15, 237
  epithelium of, 240
  radius of curvature of, 241, 247
  substantia propria of, 38, 238
Corneo-scleral junction, 237, 241 *et seq.*
Cortex, cerebral, comparison of retina with, 275
Cyclostomes, 275

Dark adaptation, 45
Descemet's membrane, 238, 240
Dilatator pupillae, 17, 128
Disc-shaped cataract, 67
Dogfish (*Acanthias*) lens plate, 48

Ectoderm, adhesions between surface and neural, 48, 52, 70, 158
  direct contact of surface and neural, 14, 22, 46
  neural, 3, 14, 17, 68 *et seq.*
  surface, 14, 16; epitrichial and nervous layers, 50

Digitized by Illinois College of Optometry Library

Ectodermal derivatives, comparison of retina with, 275
Egger's line, 185
Embryo, age-length relationships of, 13
length, 1–2 mm., 3; 2·6 mm., 8; 3·2 mm., 10; 4 mm., 10, 14, 18, 46, 135, 142; 4·5 mm., 20, 47, 159; 5 mm., 48, 74, 161, 199; 5·5 mm., 21 7 mm., 51; 7·5 mm., 24, 135; 10 mm., 30, 53, 77, 161; 12 mm., 54, 82, 142, 164, 277; 13 mm., 31, 54, 136, 164, 194; 16 mm., 195; 17 mm., 85, 137; 18 mm., 38, 196, 239; 19 mm., 139; 21 mm., 88; 25 mm., 140, 144, 243, 277; 26 mm., 167, 215; 35 mm., 171, 249; 48 mm., 39, 90, 121, 144, 172, 180, 244, 278; 65 mm., 33, 120, 122, 173, 218, 245; 75 mm., 278; 110 mm., 117, 177, 186, 228; 150 mm., 123; 170 mm., 99, 118; 180 mm., 232; 230 mm., 127; 250 mm., 100
Embryonic plate, 1
Embryos, transparency of, 39
Episclera, 246
External limiting membrane, 81, 93, 103
Extra-embryonic coelom, 2
Extra-ocular blood system, 37
Extrinsic eye muscles, 39, 253 *et seq.*
Eye, at birth, 41
phylogeny of, 42, 268 *et seq.*
rotation of, during development, 44

Faisceau isthmique, 179 *et seq.*
Fibres of Müller, first appearance of, 77
Foetal fissure, 22, 24 *et seq.*
closure of, 31, 105 *et seq.*
Foetal ocular cleft, *see* Foetal fissure
Fore-brain, 12, 142, 277
Fovea centralis, 44, 110 *et seq.*
Fovea lentis, *see* Lens pit
Frog embryo, 23
Frog, retina of, 275
Fuch's cleft, 222
Fuch's spur, 127

Ganglion cells, 87, 90, 92, 96, 100, 112
first appearance of, 87
Ganoid fish, 268
Gasserian ganglion, 42, 263
Gland, of Moll, 16, 263
of Zeiss, 16, 263
Glial sheath of hyaloid artery, 231
Granular layers, *see* Nuclear layers
Gut, fore, 2, 5
hind 2, 5

Hair bulbs, 261
Harderian gland, 261
Head cavities, 253
Head fold, 2, 4
Hind-brain, 12
Horizontal cells, 81, 98, 271
Hyaloid artery, *see* Artery, hyaloid
Hyaloid membrane, 184

Infra-orbital plexus, 193, 198
Inner cell mass, 2
Inner neuroblastic layer, 80, 87
Inter-sphincteric plexus, 219
Internal limiting membrane, 81, 82, 84, 89, 92, 96, 166 *et seq.*
Intra-embryonic mesoblast, 2
Intra-ocular blood system, 37, 203 *et seq.*
Intrinsic eye muscles, 17, 34, 123, 125, 128, 235
Invagination, *see* Primary optic vesicle
Invertebrate eye, 9
Iris, ectodermal portion of, 33, 119 *et seq.*
lesser circle of, 224
major circle of, 197, 228, 243, 244
mesodermal portion of, 38, 190 *et seq.*
muscles of, 34, 123, 220 *et seq.*
pigment in stroma of, 227
stroma of, 17, 219

Krause's glands, 260

Lacerta agilis, 56
Lacrimal apparatus, 255 *et seq.*
Lacrimal canaliculi, 259
Lacrimal gland, 262
Lacus lacrimalis, 260
Lamina suprachoroidea, 39, 200
chromatophores of, 251
Lashes, 263
Layer of Chiewitz, 80, 87, 89, 92, 95, 112, 270
Lens, 15, 30, 46 *et seq.*
equatorial section of, 56
in embryo of, 100 mm., 57; of 26 mm., 58; of 35 mm., 60; of 48 mm., 61; of 65 mm., 62
nuclei of, 64
Lens capsule (hyaline), 54, 183
(vascular), *see* Tunica vasculosa lentis
Lens epithelium, 53
Lens fibres, 31, 53
primary, 56
secondary, 56 *et seq.*
Lens pit, 19, 22, 48
Lens plate, 19, 46, of *Acanthias*, 48
Lens stalk, 27
Lens sutures, 31, 58, 64
Lens vesicle, 27, 51
separation of, 52
Lenticonus anterior, 30
Levator palpebrae superioris, 254
Lids, 15, 255 *et seq.*
Limiting membrane, external, *see* external limiting membrane
internal, *see* internal limiting membrane

Digitized by Illinois College of Optometry Library

Macula lutea, 110 *et seq.*
of birds, 270
Mammalian eye, 269
Mammillation of retina and choroid, 269
Mandibular arch, 12
Marginal bundle of vitreous, *see Faisceau isthmique*
Marginal layer of retina, 68, 76, 81
Marginal sinus, 121 *et seq.*
Maxillary process, 12, 42, 256, 264
Medullary ridge, 3
Meibomian glands, 16, 263
Mesencephalon, *see* Mid-brain
Mesoderm, associated, 16, 34, 190 *et seq.*
paraxial, 5, 12, 16, 43, 263
visceral, 5, 12, 16, 43, 263
Michel's spur, 127
Microphthalmia, 29
Mid-brain, 12
Mitosis, in lens plate, 48
in retina, 69, 71, 105
Molecular layer, inner, first appearance of, 96
outer, first appearance of, 97
Moll, gland of, 16, 263
Morula, 2
Müller, fibres of, 81, 82, 84, 87, 89, 92
early appearance of, 77
Muscles, extrinsic, 39, 253
intrinsic, 17, 125, 128, 235
Myelination, of optic nerve, 42
Myotome, *see* Somite
Myotome cavity, 6

Nerve, 5th cranial, 43
optic, *see* Optic nerve
Nerve fibre layer, 87, 89, 90, 96, 100
first appearance of, 87
Neural groove, 3, 5, 7
Neural ridge, 3, 6
Neurenteric canal, 3
Neuroblastic layers, outer and inner, 80 *et seq.*
Nuclear layer, inner (first appearance of), 82

Optic axes, angle between, 42, 263 *et seq.*
Optic chiasma, 134, 142 *et seq.*
Optic cup, 21, 68
Optic nerve, 17, 134
vessels of, 233
Optic outgrowth, 5
Optic pits, 6
Optic stalk, 12, 17, 19, 26, 32, 134
Ora serrata, 116
Orbicularis palpebrarum, 255
Orbiculus ciliaris, 236
Orbit, 253 *et seq.*
bony walls of, 267
Orbital vessels, 190 *et seq.*
Outer canthus, 258
Outer neuroblastic layer, 80 *et seq.*
Papilla nervi optici primitiva seu epithelialis, *see* Primitive epithelial papilla
Pars ciliaris retinae, 68, 115 *et seq.*
pars plana, 34, 116
pars plicata, 68, 115, 184
Pars iridica retinae, *see* Iris, ectodermal portion
Pars optica retinae, differentiation of, 68 *et seq.*
adult, 100
early capillary vasculisation of, 72
plan of differentiation of, 81, 106, 133
ratio of thickness of inner to outer layer, 76, 81, 91, 96, 98, 101, 104
Pecten, 109, 269
Petromyzon fluviatilis, 274
Phylogenetic development, 268 *et seq.*
Pigment, of choroid, 202
of iris stroma, 227
"pigment spot" of *Amphioxus*, 10
pigmented epithelium, of iris, 17, 33, 121, 123, 129; of ciliary process, 17, 118; of retina, 17, 78; of retina, processes from, 271
Placode, 8
Plica semilunaris, 260
Pluripotentiality of cells, 28
Primary germinal layers, 1
Primary optic vesicle, 1, 10
cavity of, 17, 31, 121
invagination of, 21, 23
transplantation of, 23
Primitive epithelial papilla, 26, 32
Prosencephalon, *see* Fore-brain
Pterygoid, 42, 266
Pupil, size of, during development, 130
Pupillary membrane, 217 *et seq.*
atrophy of, 221

Rathke's pouch, 142
Recessus opticus, 142
Reduplication cataract, 67
Retina, *see* Pars optica retinae
Rhombencephalon, *see* Hind-brain
Riolan's muscle, 255
Rodents, 208
Rods and cones, 92, 101
first appearance of, 92

Salamander, 24
Sauropsida, 109, 270, 272
Sauropsidan vitreous, 44
Schlemm's canal, 243, 246
Scleral spur, 245
Sclerotic, 39, 237, 249 *et seq.*
Secondary optic vesicle, *see* Optic cup
Segmentation cells, 2
Sepia, 9
Slit-lamp appearances, 37, 64, 214, 220, 222, 224
Somite, 6, 253
Sphincter pupillae, 17, 125 *et seq.*
Stroma of iris, *see* Iris, stroma

Digitized by Illinois College of Optometry Library

Sub-sphincteric plexus, 219, 220
Supra-orbital plexus, 193, 198
Suspensory ligament of lens, 17, 151, 182 *et seq.*
Synoptic comparison of ocular with general development, 281

Tail fold, 2, 4
Tapetum, 269
Tenon, capsule of, 255
Tunica vasculosa lentis, 17, 37, 167, 203 *et seq.*
  anterior portion of, 206, 216
  lateral portion of, 205, 214
  posterior portion of, 206, 211
Tunica vasculosa retinae, 209

Vasa hyaloidea propria, 37, 167, 208, 212
Vascular capsule of lens, *see* Tunica vasculosa lentis
Vascular mesoderm, entering optic cup, 49, 75
Vein, central, of retina, 37, 230
  vortex, 194
  superior ophthalmic, 197
  inferior ophthalmic, 197
Venae vorticosae, *see* Vein, vortex
Vertebrate eye, derivation of from invertebrate, 9
Vessels: annular vessel, 36, 192, 197, 198
  anterior cerebral plexus, 192
  arteria centralis retinae, 37, 73, 197, 230 *et seq.*
  arteria ophthalmica interna, 194, 198
  central vein of retina, 37, 230
  common ciliary artery, 196
  hyaloid artery, 22, 31, 36, 192, 203, 213 230, 232
  inferior ophthalmic vein, 197
  internal carotid artery, 193, 195, 198
  long ciliary artery, 197
  nasal ciliary artery, 196
  of choroid, 198 *et seq.*
  of ciliary body, 227
  of iris, 216 *et seq.*
  of optic nerve, 233
  of orbit, 190 *et seq.*
  of retina, 37, 73, 74, 197, 203, 230
  posterior ciliary artery, 197, 233
  superior ophthalmic vein, 197
  temporal long ciliary artery, 196
  vortex vein, 194
Vitreous, 151 *et seq.*
  anterior, 238
  in birds, 162
  post-natal development of, 187
  primary, 163, 172
  secondary, 165, 171
  tertiary, 179 *et seq.*

Zeiss, glands of, 263
Zinn, circle of, 233
Zonule of, *see* Suspensory ligament of lens

CAMBRIDGE: PRINTED BY W. LEWIS, M.A., AT THE UNIVERSITY PRESS

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library

LIBRARY
of the
NORTHERN ILLINOIS
COLLEGE OF OPTOMETRY

Digitized by Illinois College of Optometry Library

546



QM615
.E8M3
1928

113884

546
c.2

Digitized by Illinois College of Optometry Library

Digitized by Illinois College of Optometry Library